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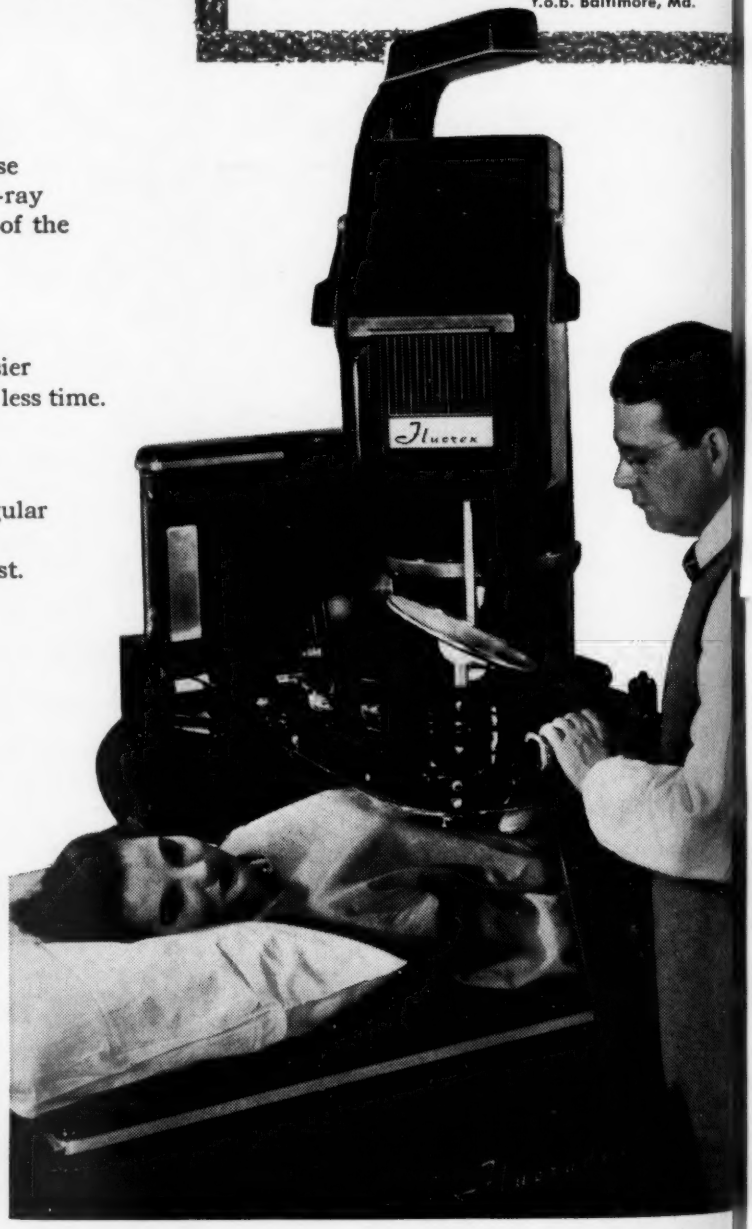

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FOCAL PULMONARY HEMOSIDEROSIS IN RHEUMATIC HEART DISEASE

By MICHAEL J. ESPOSITO, M.D.

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NEW YORK, NEW YORK

PULMONARY hemosiderosis refers to the intra-alveolar deposition of the iron-containing pigment, hemosiderin. This relatively insoluble pigment is derived from the decomposition of extravasated red blood cells, and is found principally within phagocytic cells. Alveolar macrophages laden with the yellow-brown granules of hemosiderin are a conspicuous feature of chronic passive congestion of the lungs, and for this reason they have long been called "heart failure cells." In most instances of chronic passive congestion these cells are scattered throughout the alveoli (Fig. 1*A*); however, it is not uncommon at times for the pigmented macrophages to appear in small compact foci. Such small nodular aggregates may on occasion attain both sufficient size and number to produce recognizable densities on the roentgenogram. This occurs in two distinct clinical states:

(1) In idiopathic pulmonary hemosiderosis,[2,9,27] a frequently fatal disease of unknown etiology seen almost exclusively in children, and characterized by recurrent episodes of fever, dyspnea, cyanosis, hemoptysis, and anemia.

(2) In chronic failure of the left heart due to any cause, but almost invariably as the result of rheumatic heart disease with mitral stenosis.

Rosenhagen,[18] in 1928, first drew attention to this roentgenologic feature of rheumatic heart disease and also described the histopathology. Corroborative reports followed,[1,15,17] but sixteen years elapsed before the first antemortem diagnosis was made by Park.[21] In recent years publications relative to this pulmonary complication of mitral stenosis have begun to appear with increased frequency. The large majority have appeared in the foreign literature, particularly the British, and of these the most notable have been the series of Lendrum, Scott and Park.[11,12,21]

In this country there have been surprisingly few reports concerning focal pulmonary hemosiderosis. Parker and Weiss[14] in their detailed analysis of the pulmonary changes in mitral stenosis fail to mention it. Later, Weiss[24] in a lecture before the New York Academy of Medicine made reference to the entity, but did not cite any cases. In 1944, Hurst, Bassin and Levine[10] described 5 cases of mitral stenosis associated with

miliary densities in the lung. A year later Ryder and Reineke[19] reported a comparable case simulating early silicosis. A comprehensive review was presented by Pendergrass, Lame and Ostrum in 1949,[16] at which time they reported 6 cases, including 4 with postmortem study. Other works since then have been limited to case reports by Sahn and Levine[20] and Wier *et al.*[26] The latter deals particularly with the cardiopulmonary physiological aspects of the condition.

Focal hemosiderosis is rare, at least roentgenographically, to judge from the paucity of reported cases. Park,[21] in a review of the chest roentgenograms of over 200 cases of mitral stenosis uncovered only 2 possible examples. That it is not uncommon histopathologically is attested to by the 26 cases collected by Lendrum, Scott and Park,[12] some of which were evident roentgenographically. A few authors[6,20] have suggested that the roentgenographic incidence is very likely higher than would appear from the number of cases in the literature. This contention has recently been strengthened by the observation of Baker *et al.*[3] of 5 patients with unquestionable focal hemosiderosis among 50 patients subjected to mitral valvotomy.

In the present study 100 autopsied cases of severe rheumatic heart disease were analyzed to determine the incidence of focal hemosiderosis both histopathologically and roentgenologically and to observe, if possible, the size at which the nodules became perceptible on the routine roentgenogram. An endeavor was also made to correlate the clinical and pathological findings.

The material was obtained from cases autopsied at the New York Hospital in little less than an eight year period between 1945 and 1953. During this time there were 3,294 autopsies with 233 diagnoses of rheumatic heart disease. In 133, the diagnosis was merely an accessory one; all such cases of minor valvular involvement with little structural change were excluded. In the remaining 100 cases which constitute the basis for this report, rheumatic heart disease was not necessarily the cause of death, but it was a major finding, manifested primarily by a severe valvular disturbance.

RESULTS

Review of the lung sections in the 100 cases disclosed 28 examples of focal hemosiderosis. These ranged from microscopic collections of hemosiderin-laden macrophages filling three to four alveoli, to irregular nodular aggregates measuring 1 to 3 mm. in largest diameter. The positive cases were divided into early and advanced groups on the basis of size. The advanced group, which consisted of 6 cases, exhibited masses of macrophages 1 to 3 mm. in diameter, all of which were easily visible to the naked eye on the histological section. The early group was comprised of 22 cases in which the foci measured less than 1 mm. in diameter. The 72 negative cases showed a wide variation in the number of hemosiderin-filled macrophages contained within the alveoli, and although often extremely abundant, in none were the histiocytes arranged in a focal fashion.

Study of the available roentgenograms revealed focal hemosiderosis in 5 of the advanced cases. Many of the early cases showed pulmonary congestion. At times this was intense enough to impart a somewhat nodular appearance to the central portion of the lungs. Similar appearing films were encountered in the negative group, so that the phenomenon could be attributed entirely to the vascular exaggeration.

There was nothing to distinguish the individual cases on clinical grounds, although the average age was younger and hemoptysis was more common in the group with focal deposits.

Advanced Cases. There were 4 males between the ages of thirty and forty-four years and 2 females aged forty-nine and sixty-two. The duration of known heart disease varied from five to thirty years. Hemoptysis, including blood-stained sputum as well as frank bleeding, was recorded

in 4 instances and in 2 patients it was a prominent clinical feature. Electrocardiograms revealed auricular fibrillation in 5 cases and right axis deviation was seen an equal number of times. Five patients died as a result of cardiac decompensation following repeated bouts of failure. One patient was entirely asymptomatic without evidence of decompensation, when death occurred suddenly as the result of a mesenteric thrombosis.

At autopsy there was a marked mitral stenosis present in all cases and in one there was an associated aortic stenosis. No cardiac catheterizations were performed in this group, but all showed right ventricular hypertrophy, indicative of an increased pressure in the lesser circulation. Another manifestation of this increased tension was the sclerosis consistently observed in the pulmonary arterioles.

Histopathologically the outstanding finding was the large nodular accumulations of pigmented macrophages that readily reacted with potassium ferrocyanide to give a markedly positive Prussian blue reaction. These were situated haphazardly without obvious relation to vessels or bronchi. The macrophages tended to be tightly packed in the alveolar spaces with considerable fibrosis of the interposed alveolar septa. There were relatively few "heart failure cells" in alveoli outside the nodules, and sections stained for iron showed only a negligible uptake in the interstitial tissues. In 5 cases there was chronic passive congestion associated with some interstitial fibrosis and in all there was thickening of the pulmonary arterioles. The patient who had been asymptomatic prior to her sudden death had no pulmonary congestion and the alveoli between the nodules were remarkably normal.

The roentgenograms revealed discrete nodules measuring 2 to 5 mm. in diameter in 5 cases. In the sixth case, congestive changes were prominent, and no punctate densities could be clearly differentiated from the vascular engorgement. The nodules were best visible in the mid-zones, but extended into both upper and lower lung fields. The apices were spared in all but one case. There was cardiac enlargement with evidence of mitral disease, and some degree of pulmonary congestion in 5 cases. In one case the heart was not obviously enlarged and there was no prominence of the vascular markings at all, although the lung fields revealed a striking miliary nodularity. Three of these cases are briefly summarized below (Cases I, II, and III).

Early Cases. There were 13 females and 9 males with hemosiderin deposits measuring less than 1 mm. in greatest diameter. This is in contrast to the predominance of males in the advanced group and is at variance with the very high percentage of males among cases reported in the literature. Thirteen of the patients were in the third and fourth decades. There was one child aged ten, and the remaining 8 patients ranged in age from forty-three to sixty-seven years.

The duration of the disease, measured from the time cardiac involvement became apparent, varied from an extreme of months to twenty-five years. Hemoptysis occurred in 11 cases and in 4 instances was particularly troublesome. Mitral stenosis was present in 9 of the patients with hemoptysis, whereas in 2, aortic stenosis was the essential cardiac lesion. Electrocardiograms revealed auricular fibrillation in 13 cases and right axis deviation occurred in still a greater number.

At necropsy, all cases exhibited some degree of right ventricular hypertrophy. Mitral stenosis was evident in 18 cases. In 2 of these there was an associated aortic stenosis, and 3 others had significant involvement of the tricuspid valve with some stenosis. In none did the tricuspid stenosis approach the severity of the mitral stenosis. Four cases had calcific aortic stenosis with only minor stigmata of rheumatic involvement of other valves.

The histopathological appearance of the lungs in this group was analogous to that in the advanced group, with the exception of the hemosiderin collections. These were

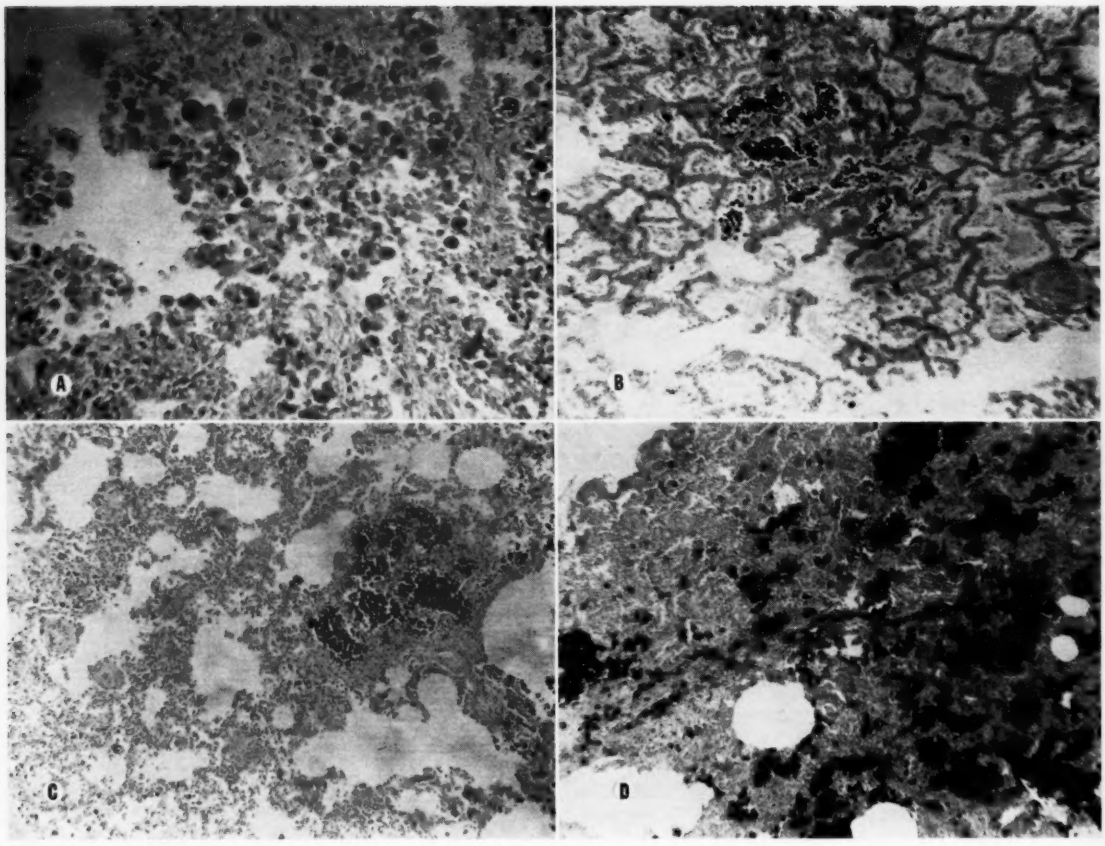

Fig. 1. Examples of chronic passive congestion of the lungs.

(*A*) Photomicrograph showing the usual picture with many scattered dark staining "heart failure cells." Patient with aortic, mitral and tricuspid valvulitis. (NYH 14187) Hematoxylin and eosin. 150×.

(*B*) Early focal hemosiderosis with loosely congregated intra-alveolar pigmented macrophages. Patient with mitral stenosis. (NYH 14829) Hematoxylin and eosin. 45×.

(*C*) Early focal hemosiderosis with tightly packed macrophages and fibrosis of the alveolar septa resulting in the formation of a nodule. Patient with mitral stenosis. (NYH 12281) Hematoxylin and eosin. 45×.

(*D*) Another early case of focal hemosiderosis in a patient with aortic stenosis of rheumatic origin. Despite the innumerable subpleural macrophages which have taken up the stain for iron, there were only minor clumps elsewhere and the roentgenogram was unremarkable. (NYH 13154) Perls' method and Masson red. 45×.

of course smaller but, in addition, the macrophages were often not as tightly packed and there was little or no fibrosis of the filled alveoli (Fig. 1*B*). Occasionally there was distinct nodule formation of these lesser aggregations similar to that seen in the advanced cases (Fig. 1*C*). Again the alveoli between the focal deposits of hemosiderin were relatively clear of pigmented macrophages. When present, the "heart failure cells" were heaviest immediately about the periphery of the nodule and hence appeared to be converging towards it. Subpleural collections of macrophages were common. In one case enormous numbers occurred just below the pleura (Fig. 1*D*), despite the presence of only minor clumps elsewhere in the parenchyma.

Roentgenograms were available in all but 2 cases. Careful scrutiny of these films failed to disclose any clear cut examples of focal hemosiderosis. Many showed a somewhat nodular character to the lung fields, but this could not be clearly disso-

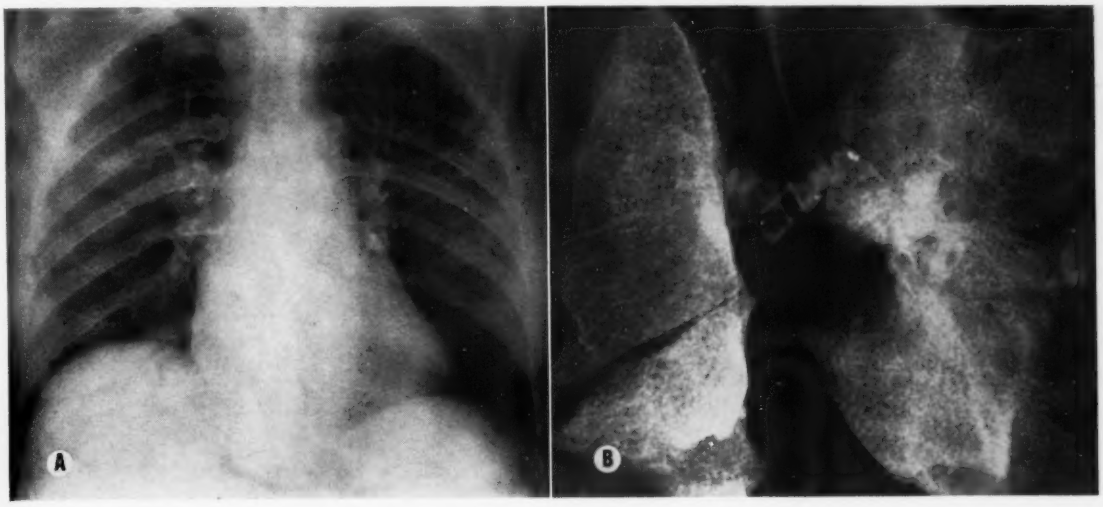

FIG. 2. Case I. (*A*) Anteroposterior film of the chest reveals a widespread miliary process. The irregular nodules vary from 2 to 4 mm. The heart is unremarkable. (*B*) Roentgenogram taken at the time of necropsy shows the diffuse and somewhat confluent radiopacities.

ciated from the pulmonary congestion.

Negative Cases. There were 39 males and 33 females. Nineteen were below the age of forty; 21 were in the fifth decade; 32 were beyond the age of fifty. Hemoptysis occurred in 18 cases. Except for the increase in average age and lessened incidence of hemoptysis, the clinical features in no way differed from those manifested by the positive cases.

Similarly, the autopsy findings closely paralleled those of the previous groups. The heart involvement was equally severe in most cases. There were 51 patients with mitral stenosis. Many of these had associated lesions, including 15 with aortic stenosis. As for the remaining patients, in 14 a stenotic aortic valve was the major finding and in 7 there was an aortic, mitral and tricuspid valvulitis without narrowing of any valve orifice. Right ventricular hypertrophy contributed to the cardiomegaly in nearly every case.

The pathological findings in the lungs were identical to those observed in the other groups except for the absence of focal hemosiderin deposits.

It was possible to review the roentgenograms in 49 of these cases. There were none that resembled the more advanced cases of focal hemosiderosis. Many showed congestive changes with a suggestion of nodularity. As in the early cases this pseudonodulation could not be divorced from the vascular markings.

Additional Cases. Three additional examples of advanced focal hemosiderosis with mitral stenosis, not falling within the scope of the series under discussion, were uncovered during this investigation and are herein included. There were 2 males aged twenty-three and twenty-four and 1 female aged forty-two. All had rheumatic fever in childhood and heart involvement had been present for eleven, sixteen and twenty-eight years respectively. There was auricular fibrillation and hemoptysis in all cases and in 2 of the patients the hemorrhages were repeated. The roentgenogram of the chest in each instance revealed diffuse involvement of the lungs by pulmonary nodules measuring 2 to 4 mm. In 2 cases the densities extended into the apices. There was no autopsy performed in 1 case; however, the clinical history and roentgenologic appearance of the lungs leave little doubt as to the diagnosis. In the other 2 cases the diagnosis was verified at autopsy and these are included below (Cases IV and V).

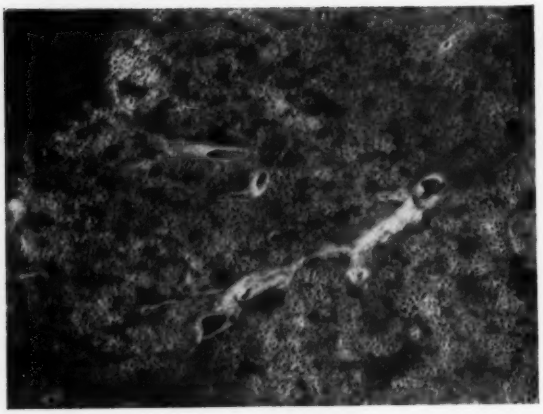

Fig. 3. Case 1. Close view of the unstained lung following fixation (Kaiserling 1 solution) shows clearly the foci of hemosiderin that measure about 3 mm. in diameter.

REPORT OF CASES

Case 1 (NYH 654 928). M.R., a white female, aged sixty-two, entered the hospital because of the acute onset of severe mid-abdominal pain, associated with vomiting, abdominal distention and tenderness in all quadrants. Pertinent physical findings were auricular fibrillation and a silent tender abdomen with a purplish tint to the skin. The nature of her heart ailment was unknown to her despite the fact that she had been receiving digitalis for the past seven years. She was gravely ill on admission and died shortly thereafter from what was thought to be a mesenteric thrombosis.

Roentgenograms (Fig. 2). Anteroposterior film of the chest with the patient recumbent reveals a uniform distribution of 2 to 4 mm. nodules throughout all lung fields but the apices. The heart is not obviously enlarged nor is the configuration particularly striking. There is no pulmonary congestion. Some calcification is seen in the aortic arch and in the left hilus. A section of the isolated lungs roentgenographed at the time of autopsy discloses a confluence of miliary radiopacities.

Autopsy (NYH 15023) (1) Thrombosis of the superior mesenteric arteries with infarction of the intestines. (2) Rheumatic heart disease: The heart weighs 420 grams; the mitral valve is markedly stenotic; the auricles and the right ventricle are dilated and hypertrophied. The lungs are subcrepitant, and scattered throughout the parenchyma are numerous 2 to 3 mm. islands of brown pigment (Fig. 3). These measure 1 to 2 mm. on the histological section and microscopically are dense aggregations of hemosiderin-laden macrophages that fill 4 to 20 alveoli to form a nodule (Fig. 4). There is some fibrous tissue reaction in the region of the nodules. They are unrelated to blood vessels or bronchi. Elsewhere the alveoli are clear and show no evidence of passive congestion. Minimal amounts of hemosiderin are present in the interstitial tissues. There is thickening of blood vessels.

Comment. The age of the patient is noteworthy, as is the fact that advanced focal

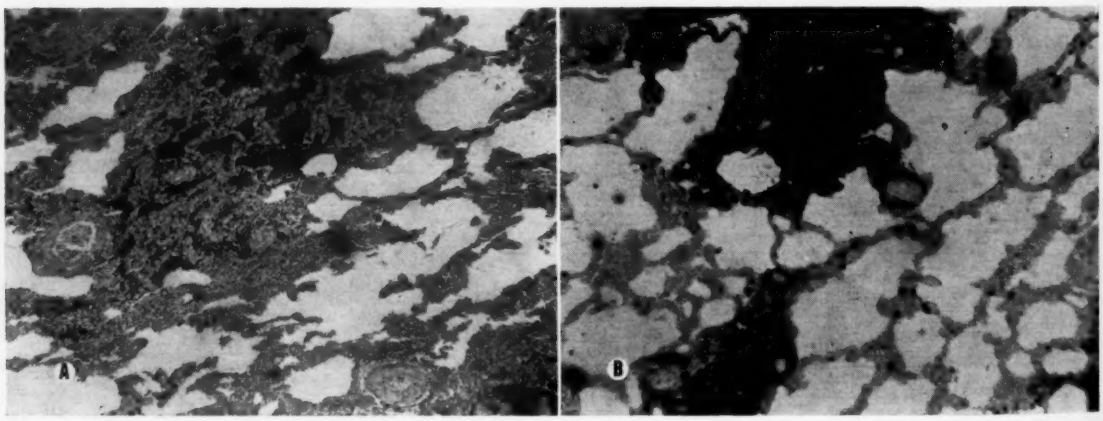

Fig. 4. Case 1. (*A*) Photomicrograph showing the well demarcated nodule of advanced focal hemosiderosis. Fibrosis is limited to the alveoli incorporated into the nodule and there is no passive congestion. Hematoxylin and eosin. 45×. (*B*) Section stained for iron shows an intense reaction in the region of the nodules but only minimal amounts of Prussian blue in the interstitial tissues. The alveoli between the nodules are normal. Perls' method and hematoxylin. 45×.

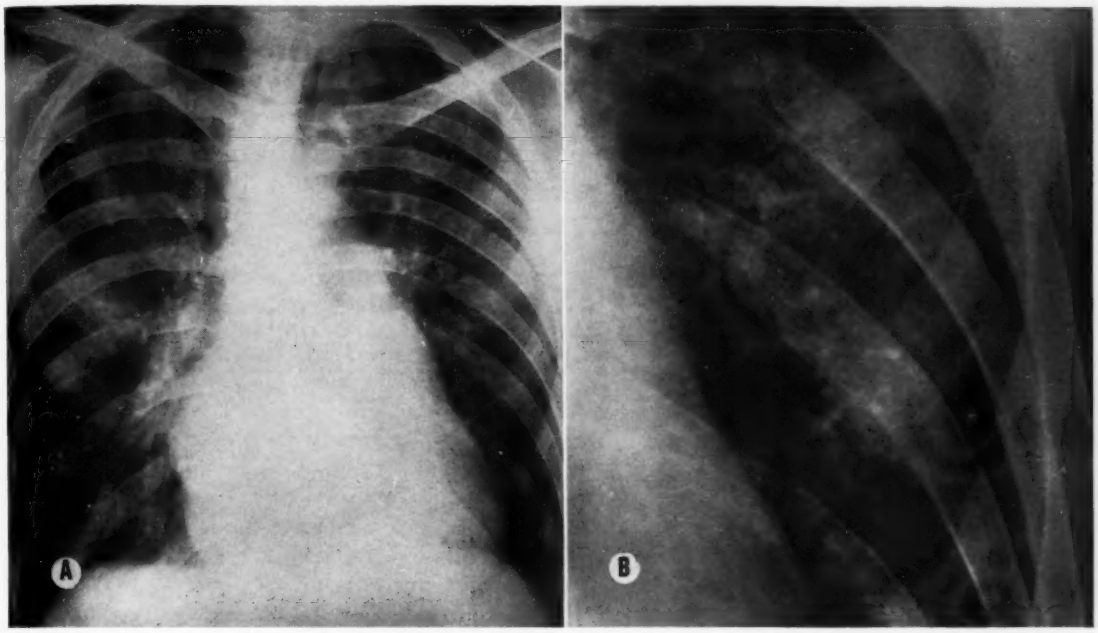

Fig. 5. Case II. (*A*) The granular densities are partially obscured by the vascular markings. There are only a few nodules in the right lower lung field and these appear to be calcified. The heart shows evidence of a double mitral lesion. (*B*) Enlargement of the left mid-lung field shows the granular infiltration.

hemosiderosis may be present in the completely compensated cardiac patient. Roentgenographically the marked nodularity, minimal heart changes and complete absence of pulmonary congestion is extraordinary. Likewise histopathologically, the normality of the alveoli between the nodules is remarkable.

Case II (NYH 541 193). R.N., a white man, aged thirty-three, developed rheumatic fever at the age of twenty-five. Three years later he was digitalized because of heart failure. Hemoptysis occurred frequently. Heart findings were those of mitral stenosis, mitral insufficiency, and tricuspid insufficiency. Electrocardiograms showed auricular fibrillation and right axis deviation. Death occurred five years after the initial episode of failure, a total of eight years from the onset of his rheumatic attack.

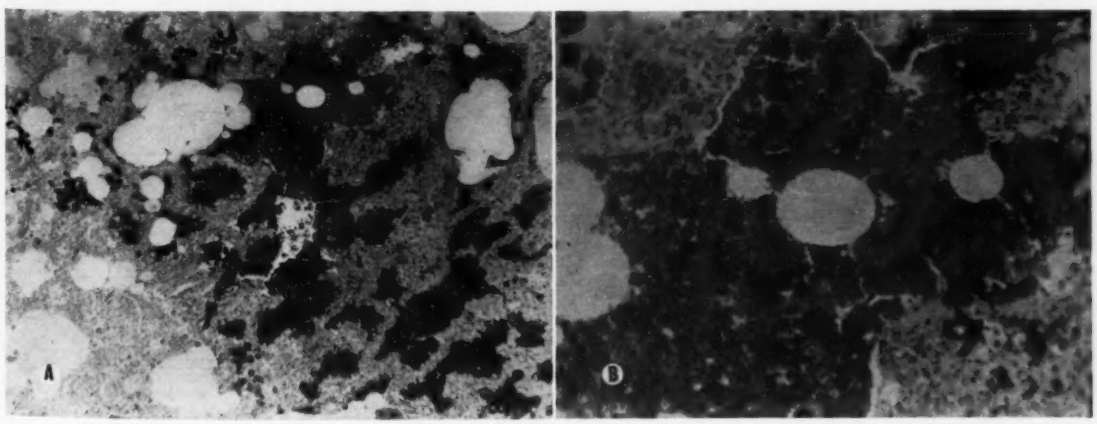

Fig. 6. Case II. (*A*) Collection of pigmented macrophages measuring a little over 1 mm. in greatest diameter. Hematoxylin and eosin. 45×. (*B*) Higher magnification shows the granules of hemosiderin within the histiocytes. Hematoxylin and eosin. 150×.

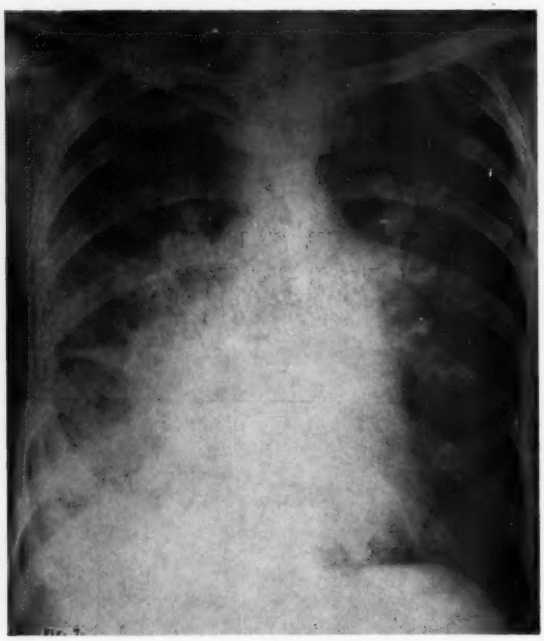

Fig. 7. Case III. The pulmonary nodules measure from 3 to 5 mm. in diameter. The apical involvement is not evident on the reproduction. The heart is enlarged and the pulmonary vessels at the right lung root are quite prominent. There is a pleural effusion on the right.

Roentgenogram (Fig. 5). There is some pulmonary congestion which tends to obscure the fine nodular densities that are limited for the most part to the mid-zones. The apices are spared and the lesions are only sparsely distributed at the bases. The few that are visible in the right lower lung appear to be calcific in nature. The heart is quite large; the left atrium elevates the left main stem bronchus and extends beyond the right heart border.

Autopsy (NYH 13655). The heart weighs 525 grams. There is an adhesive pericarditis. The mitral valve ring and cusps are calcified and only a slit-like orifice remains. The other valves show only minimal thickening. The chambers of the heart are enlarged, with the left atrium and right ventricle showing the greatest increase. The lungs are edematous and congested with some areas of infarction. Microscopically there is diffuse capillary and vascular engorgement with scattered intra-alveolar hemorrhages. There are multiple foci of coalescent macrophages containing granules of brown pigment. The largest of these collections measures approximately 1 mm. in greatest diameter (Fig. 6). There is some interstitial fibrosis in the region of the macrophages. The pulmonary arteries and arterioles are thickened.

Comment. Development of the condition in a young man with mitral disease complicated by recurrent hemoptyses is in keeping with most reported cases. The duration of his illness is of interest, and shows that cardiac involvement need not be extremely prolonged for the production of these nodules.

Case III (NYH 414 363). R.L., a white man, aged forty-four, gave no history of rheumatic fever but at age fourteen a murmur was detected. Exertional dyspnea had existed for the past twenty years, and he had been taking digitalis for a period of five years. Cough, orthopnea, cyanosis, and ankle edema necessitated admission. The heart was enlarged with a normal sinus rhythm. A short systolic and a diastolic rumble were audible at the apex. The lungs revealed widespread rales. The patient became lethargic, began to cough up small amounts of blood and died.

Roentgenogram (Fig. 7). There are nodular densities scattered throughout both lungs. These measure 3 to 5 mm. in diameter and extend from the apices to the bases. There is a pleural effusion on the right, which extends up to, and involves, the straight fissure. The heart shows prominence of the pulmonary artery seg-

Fig. 8. Case III. Photograph taken at necropsy shows the discrete and evenly distributed hemosiderin nodules responsible for the densities seen on the roentgenogram.

ment and there is marked enlargement of the pulmonary vessels at the right lung root.

Autopsy (NYH 11875). The heart weighs 430 grams. The mitral valve is stenotic and presents a "button-hole" appearance. There is minimal thickening of the leaflets of the tricuspid and aortic valves. The right side of the heart and the left auricle show considerable hypertrophy and dilatation. The lungs are firmer than normal and have a brownish tinge. On cut surface there are 3 to 4 mm. nodules of brown-black material evenly distributed in all lobes (Fig. 8). These take up the stain for iron and measure a full 3 mm. in diameter on the tissue section (Fig. 9). On microscopic study they are composed of innumerable hemosiderin-laden macrophages crowded into contiguous alveoli (Fig. 10). The alveolar septa are obliterated for the most part. There is evidence of chronic passive congestion and the small blood vessels are thickened with fibrosis and show intimal proliferation.

Comment. This patient with a history of heart disease for thirty years represents the most extreme example encountered. Hemoptysis was not a paramount feature clinically, and occurred only terminally. This terminal bleeding can hardly explain the tremendous deposits of hemosiderin which undoubtedly accumulated over many years. It is apparent that considerable intra-alveolar hemorrhage may occur over long periods without hemoptysis.

Case IV (NYH 157 077). F.S., a white woman, aged forty-two, had rheumatic fever at the age of fourteen, at which time a diagnosis

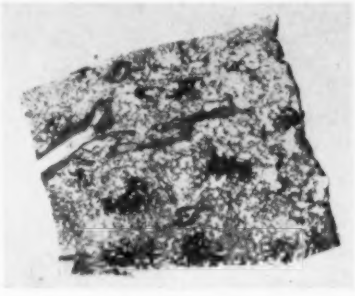

Fig. 9. Case III. Histopathological section stained for iron shows the formation of Prussian blue localized to the masses of hemosiderin-containing macrophages. These measure a full 3 mm. in diameter. Perls' method and Masson red. 2×.

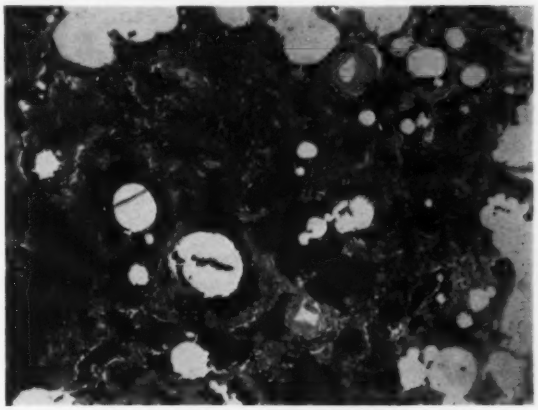

Fig. 10. Case III. Photomicrograph of nodule shown in Figure 9. The formation of Prussian blue is so marked that lung detail is obscured. Perls' method and Masson red. 45×.

of rheumatic heart disease was made. Four years later she experienced dyspnea accompanied by hemoptysis. Subsequently there were numerous episodes of failure with much expectoration of blood. Electrocardiograms revealed auricular fibrillation and right axis deviation. In 1951 the patient died in congestive failure.

Roentgenograms (Fig. 11). The initial film taken in 1937 reveals a mitral configuration of the heart with pulmonary congestion. The lung markings show some granularity that might be passed over as part of the vascular pattern, but in retrospect is believed definitely due to early hemosiderosis. Films taken three, five, and thirteen years later show a very distinct nodular infiltration of a miliary character. On the earlier studies the nodules are primarily midzonal with sparing of the apices and bases but on the most recent one they have progressed in size and can be seen in all lung fields, except the extreme apices. As in most cases the nodules can be identified at the lung periphery where vascular shadows are at a minimum. There is enlargement of the heart with prominence of the pulmonary artery segment and left auricular appendage.

Autopsy (L.H.H. 4532). Postmortem study was performed at the Lenox Hill Hospital (New York City) and through the courtesy of Dr. R. M. Paltauf, the autopsy protocol and a small section of the lung were made available. The anatomical diagnoses were as follows: rheumatic carditis with mitral stenosis, pulmonary arteritis, chronic passive congestion of the lungs (brown induration), and pulmonary infarcts,

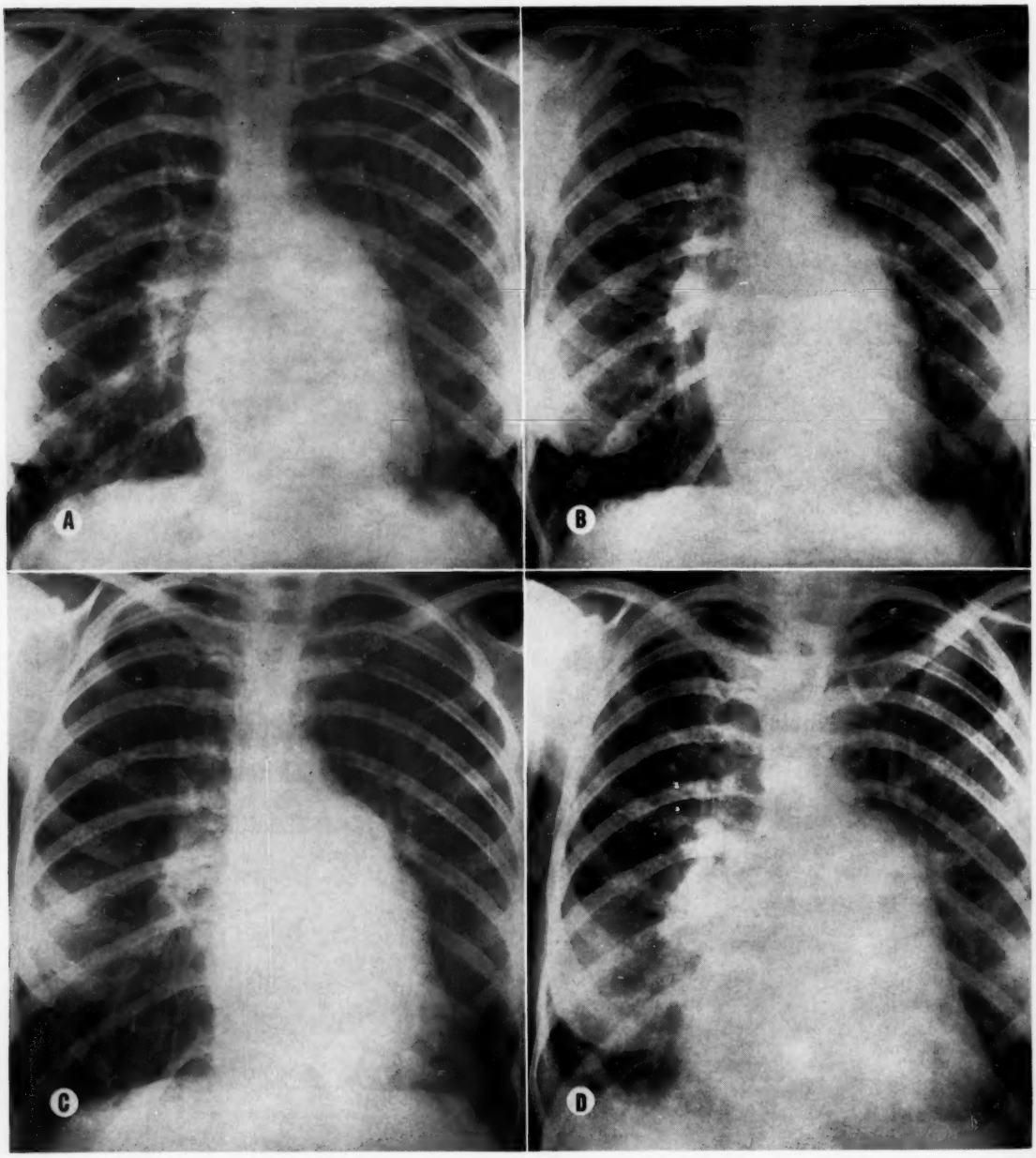

Fig. 11. Case iv. (*A*) Film taken in 1937. The heart shows a mitral configuration and there is pulmonary congestion with a nodular component best seen in the mid-zones. (*B*) Film taken in 1940. The nodules are more distinct. (*C*) Study performed in 1942 shows little change in the lungs. (*D*) Final examination in 1950 shows increase in size and extent of the nodules. The heart is larger and pulmonary congestion is more prominent.

right lower lobe. There is visible on the small tissue section a brown spot measuring just over 1 mm. in greatest diameter. Microscopically this is the typical nodule of hemosiderosis. A number of smaller foci of pigmented macrophages are present. The alveoli between hemosiderin deposits are relatively clear although the septa do show some thickening due to fibrosis. The arteries and arterioles show marked intimal and medial hyperplasia.

Comment. This patient was asympto-

matic at the time of her last roentgenogram, a total of thirteen years following the first observation of the nodules. She demonstrates well the permanence of these pulmonary deposits and emphasizes the benignity of their presence.

Case v (NYH 124 234). J.W., a white male, aged twenty-three, had rheumatic fever at the age of twelve and at the age of seventeen exhibited signs of congestive failure. He was first seen two years before death because of pulmonary edema. Examination during his final admission revealed cardiac enlargement with a totally irregular rhythm. There was a diastolic apical thrill, and murmurs indicative of mitral stenosis, mitral insufficiency and aortic insufficiency were audible. He began to raise blood-tinged sputum. Cardiac decompensation was severe and unrelenting. Heart failure became complicated by pneumonia and death ensued.

Roentgenogram (Fig. 12). The heart is huge. Congestive changes are not too marked and punctate densities varying between 2 and 4 mm. are readily apparent. These show a fairly even distribution which includes the apices. There is a pleural effusion at the left base.

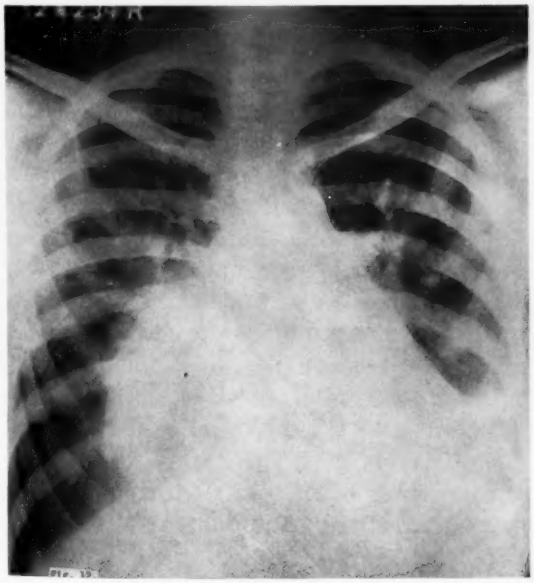

Fig. 12. Case v. There is diffuse involvement of the lungs, including the apices, by 2 to 4 mm. densities. As in most cases the nodules extend to the lung periphery beyond the confines of any significant vascular markings. The heart is huge and there is a pleural effusion on the left.

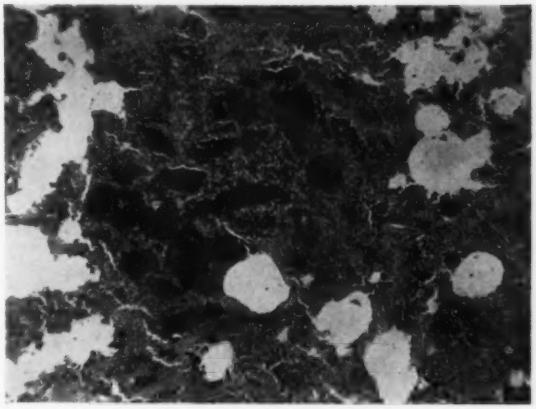

Fig. 13. Case v. Lung section confirming the diagnosis of focal hemosiderosis. Hematoxylin and eosin. 45×.

Autopsy (NYH 9310). The heart weighs 800 grams, and there is tremendous dilatation of the left auricle. Both ventricles are large with increased thickness of the wall, particularly on the right. The mitral valve is rigid and greatly thickened by fibrous tissue and calcific concretions resulting in stenosis and insufficiency. The aortic leaflets are moderately thickened and shortened and there is evidence of a regurgitation pocket in the endocardium beneath the valve. There is minimal involvement of the tri-

Fig. 14. Case v. Extra large tissue section mounted and stained for iron demonstrates the nodular foci of hemosiderin-containing macrophages that give rise to the roentgen findings. Perls' method and Masson red. 2×.

cuspid and pulmonic valves. The lungs are dark red with many small areas of consolidation. Much frothy fluid escapes from the cut surface and the consistency of the lung is uniformly leathery. Microscopic study shows chronic passive congestion with some edema and areas of bronchopneumonia. There is considerable interstitial fibrosis. Occasional "heart failure cells" are seen singly, but for the most part they are massed together in deposits measuring between 1 and 2 mm. (Fig. 13). These nodular accumulations are readily seen with the naked eye, and the amazing extent to which the iron-containing cells have infiltrated into the alveoli is best appreciated when a large tissue section has been stained especially for the iron (Fig. 14).

Comment. The absence of apical involvement in focal hemosiderosis, often utilized to distinguish the condition from miliary tuberculosis, cannot be relied upon in the more advanced cases.

DISCUSSION

Focal hemosiderosis is not as rare a complication of rheumatic heart disease as is generally believed. The total incidence in 100 cases was 28 per cent and the roentgenographic incidence 5 per cent. Small foci of hemosiderin were observed with aortic stenosis alone, but the vast majority, including all large enough to be recorded on the roentgenogram, were the result of mitral stenosis. Patients with mitral stenosis have a relatively good life expectancy, and this, coupled with their proclivity for both pulmonary hemorrhages and repeated episodes of congestive failure, makes them particularly prone to develop hemosiderosis.

There has been a predominance of young males among reported cases, which is somewhat surprising since mitral stenosis is more common in females. It may possibly be related to the greater activity ordinarily seen in young men. Among the more severe cases young males were singled out for the most part; however, when all cases were considered, there proved to be no predilection for either sex. There was a definite tendency for the condition to occur in the third and fourth decades, but patients beyond this age were by no means immune. Bradlow,[4] in a recent study of hemoptysis in mitral stenosis, has shown that it also tends to occur at an early age and without predilection for sex.

It was impossible to determine at the clinical level whether or not any given case of chronic rheumatic heart disease had focal hemosiderosis. A large percentage of the cases gave a history of hemoptysis, but there was no correlation between the degree of hemoptysis and hemosiderosis. Indeed, patients who never had any bloody sputum exhibited advanced hemosiderosis, whereas others with frequent hemoptysis showed only small numbers of pigmented macrophages. The lack of correlation does not serve to minimize the importance of hemorrhages in the production of the hemosiderin deposits, but rather indicates that hemoptysis is at best a poor index of the amount of intra-alveolar hemorrhage.

There proved to be no correlation between the duration of heart disease and the presence or the extent of focal hemosiderosis.

The basic pathologic change in focal hemosiderosis is the presence of innumerable hemosiderin-containing histiocytes that are jammed into juxtaposed alveoli. There is often considerable associated fibrosis with formation, then, of a sharply demarcated nodule. The surrounding alveoli may be perfectly normal, but usually manifest some changes of chronic passive congestion. The arterioles invariably show degenerative changes that reflect the presence of an increased pressure in the pulmonary circulation.

Pulmonary hypertension with repeated hemorrhages on a mechanical basis constitutes the fundamental disturbance in the pathogenesis of nodular hemosiderosis. Lendrum *et al.*[12] believe that the size, shape and distribution of the deposits point to the anastomosis between pulmonary and bronchial vessels in the terminal bronchiole as the source of the hemorrhages. Magarey,[13] however, has produced focal hemosiderosis in rats with endotracheal injec-

tions of blood and concludes that no focal bleeding site need be incriminated.

Not all patients with pulmonary hemorrhages exhibit deposits of hemosiderin. As Ellman and Gee[6] state, it is probably only a question of speed; fresh hemorrhages, occurring before earlier ones can be cleared by the phagocytes, allow the hemosiderin to accumulate. Strassmann[22] has shown in rabbits that erythryocytes introduced into the alveoli are ordinarily removed within twenty-four hours by the alveolar macrophages. In the presence of pulmonary edema, however, their removal is delayed with the subsequent appearance of hemosiderin-containing macrophages. According to Gumpert[8] venous congestion may cause obstruction to the lymphatic drainage of the phagocytosed red blood cells. The hemorrhages, with edema and venous congestion as possible contributing factors, readily account for the appearance of the nodules but do not explain their persistence over many years, even in the absence of any pulmonary symptomatology.

The most satisfactory explanation for the perpetuation of the nodules has been advanced by Lendrum, Scott and Park.[12] These authors have postulated that hemosiderin, unlike exogenous iron, is not an inert material, but is responsible for the fibrosis in the region of the nodules, which in turn blocks the normal drainage of the macrophages. They state, "If sufficient haemosiderin be present in a system of cognate alveoli, the iron released from this depot leads to damage and reaction in the adjacent tissue, and so strangles the lymphatic route of withdrawal."

The essential roentgenologic feature of focal hemosiderosis is a diffuse, fine, granular pulmonary nodulation. This is nearly always associated with an enlarged heart bearing a mitral configuration. The nodules are irregular in outline and on the roentgenogram generally measure between 2 and 4 mm. in greatest diameter. On occasion they may be as large as 5 mm. They are concentrated in the mid-zones but do extend towards the periphery in all directions. The apices are usually spared but in the more advanced cases this may not be so. Actually the nodules are uniformly situated throughout the lungs in most cases and the distribution evident roentgenographically is due to differences in lung volume. The nodules of hemosiderosis are constant and, once present, have never been observed to disappear or to decrease in size.

Pulmonary congestion tends to obscure the miliary nodules and is of itself able to produce a pseudonodularity in the lung fields. Fortunately, the changes are often of a transient nature. In addition, the nodularity is primarily in the parahilar areas, and fades out as the vessels course peripherally. In contradistinction to this, the aggregates of hemosiderin are often clearly visible in the outermost lung fields. It is the presence of these nodules beyond the confines of any conspicuous vascularity that is diagnostic.

There can be little doubt that many cases of focal hemosiderosis are dismissed as examples of severe pulmonary congestion, and it is the failure to differentiate the two that is chiefly responsible for its relative rarity.

It is difficult to determine the size at which the deposits become evident roentgenographically. The nodules appear larger than they actually are due to superimposition, so that the number and spatial relationships, as well as size, are governing factors. Congestive changes must be reckoned with; finally, the threshold of visibility of any miliary process will be further influenced by the composition of the nodules, the thickness of the chest wall, and the technique of exposure.

In general, it may be said that diffusely scattered hemosiderin collections of less than 1 mm. do not cast an appreciable shadow. Those measuring about 1 mm. can be identified unless congestive changes are extreme. Deposits measuring between 2 and 3 mm. in diameter give rise to a conspicuous nodulation at all times. It should be pointed out that these figures refer

to measurements taken from mounted tissue sections, realizing fully that some reduction in size has occurred as the result of tissue shrinkage during processing.

Disseminated, calcified and bony nodules occurring primarily in the lower half of the lungs is still another pulmonary manifestation of mitral stenosis.[7,25] Elkeles and Glynn,[5] in a review of this subject, excluded tuberculosis as a possible etiology, and related the nodules to a specific rheumatic pneumonia. Terplan,[23] on the other hand, has postulated that the initial disturbance in the production of these nodules is a thrombosis in the septal capillary and that the mesenchymal cells of the septa are concerned with the gradual formation of bone. A few such cases have been observed in conjunction with focal hemosiderosis and the question of the relationship between the two has naturally arisen. Some observers[6,20] believe they may represent the end stage of the organization of hemosiderin deposits. However, this contention has not been borne out by the pathological studies of Lendrum,[11] who believes that the osseous nodules originate in fibrinous casts. The large number of cases of hemosiderosis without co-existent bony nodules and the failure to demonstrate any connection between the two on histopathological grounds is strong evidence that the association is purely fortuitous.

The course of rheumatic heart disease is in no way altered by the presence of nodular hemosiderosis. The nodules are not responsible for any symptoms, nor do they adversely affect pulmonary function. They do not influence the prognosis, although in most cases the prognosis is grave because the mitral stenosis is marked. According to Baker *et al.*,[3] hemosiderosis is not a contraindication to mitral valvotomy, and its presence should in no way influence the decision of operability.

Focal hemosiderosis is of importance only when the nodules become evident roentgenographically, and then only because the roentgenologic appearance is not distinctive. In addition to simple pulmonary congestion, the differential diagnosis includes the many diseases that can produce a miliary pulmonary infiltration. The more common include miliary tuberculosis, the pneumoconioses, sarcoidosis, and metastatic carcinoma. Each of these may at times reveal certain features that are not to be expected with hemosiderosis, but in many instances the appearance will be indistinguishable. In all cases an enlarged heart, especially with a mitral silhouette, should serve to arouse one's suspicions. In the final analysis, recourse to the history and clinical status will frequently be necessary to differentiate the various conditions.

SUMMARY

Focal pulmonary hemosiderosis is not as rare a sequela of rheumatic heart disease as earlier reports would indicate. A study of one hundred necropsied cases with rheumatic heart involvement disclosed twenty-eight histopathological examples. With the exception of four early cases due to aortic narrowing, all cases were the result of mitral stenosis. Five advanced cases with focal hemosiderin collections, measuring 1 to 3 mm. on the microscopic section, revealed a very definite diffuse miliary nodulation of the lungs roentgenographically. Three additional cases with striking roentgenograms, two of which were verified at postmortem, are also reported.

Clinically, there is a high incidence of hemoptysis, but the condition presents no distinctive features. Cases occur commonly in the third and fourth decades. Although histologically no sex predilection was noted in this series, the most advanced cases tend to occur in young males, and hence they are more liable to detection by roentgen study.

The salient pathological finding is a well demarcated nodule of agglomerated pigmented macrophages produced by repeated hemorrhages; edema and venous congestion exert a favorable influence on the development of such foci. Localized fibrosis, apparently induced by the hemosiderin,

prevents escape of the phagocytes into the lymphatic channels and so perpetuates the nodule.

Since the process is a completely benign one, its importance stems solely from the fact that roentgenographically, in advanced form, it can simulate many other diseases. However, the roentgen picture is not always clear cut, and the less obvious cases can easily masquerade under the guise of pulmonary congestion.

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PULMONARY EDEMA

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RECENTLY a well trained internist asked the Department of Radiology to show him the chest films of one of his patients in the hospital. He was startled when the films presented a massive, discrete, flocculent, butterfly pattern radiating from the hila or central zones of the lungs since no pulmonary lesion was suspected clinically (Fig. 1). The first question the radiologist asked was the patient's nonprotein nitrogen. It was 136 mg. per 100 cc.

In the course of the consultation it was brought out that the patient was a twenty-one year old white female stenographer with chronic glomerular nephritis. Her general health had been poor since the age of four when she had acute glomerular nephritis. She was tired and listless, and she had suffered numerous attacks of asthma.

Two weeks before admission she felt drowsy; her sight became poor and she developed dyspnea, nausea and anorexia.

On physical examination, the blood pressure was 170/115; pulse 96; respiration 32. The patient was undernourished, chronically and acutely ill and appeared pale, drowsy and moderately dyspneic. Her breath was uriniferous. Examination of the eye-grounds revealed blurring of the disc margins, many old and recent exudates. Diminished breath sounds and moist râles at both bases posteriorly were noted on examination of the lungs. The heart appeared moderately enlarged with a forceful point of maximal impulse.

Laboratory studies included: Erythrocyte count, 2.29 million; hemoglobin, 6.0 gm.; leukocytes, 10,500; stools, guaiac positive. The urine contained 2 plus albumin. The phenolsulphonphthalein test for renal function showed no excretion after thirty minutes.

On the tenth hospital day the patient died after a generalized convulsion. Necropsy confirmed the clinical impression of chronic glomerular nephritis and pulmonary edema.

This incident and other similar experiences prompted us to make a clinical and roentgenological study of pulmonary edema with particular emphasis on the roentgen pattern of pulmonary edema and its differential diagnostic significance (Fig. 1).

CLINICAL MANIFESTATIONS OF PULMONARY EDEMA[12]

Acute pulmonary edema may begin with terrifying suddenness or may gradually develop from a mild form of paroxysmal nocturnal dyspnea which is frequently alleviated when the patient sits up or walks about. From this mild stage the patient may develop cardiac asthma manifested by considerable shortness of breath (with special difficulty in the expiratory phase), orthopnea and great anxiety.

The chronic form may be quite insidious. Some shortness of breath and cough productive of blood-tinged sputum are often noted in nephritics with pulmonary edema. Orthopnea is not always present. When the edema is central, râles may be inconstant or absent. In cases in which pulmonary edema is associated with nephritis, one frequently notes nausea, vomiting, anemia, petechiae and ecchymoses in the skin, hypertension, an elevated nonprotein nitrogen and occult or gross blood in the stools.

The pulmonary edema which we would like to stress is the subacute or chronic form which frequently exists with such subtle clinical manifestations that it may be easily overlooked by the attending physician. It has been noted that the roentgenogram of the chest is frequently the first indication of the presence of pulmonary edema.

PATHOGENESIS[4,13]

Relying on clinical observation alone, we know that most patients with pulmonary edema are cardiacs in congestive failure. Welch[14] was one of the first to investigate the cardiac mechanism of pulmonary

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edema by occluding the aorta in dogs and causing thereby acute left ventricular failure. Pulmonary edema resulted. Making a rather long jump from an acute experiment on an animal to the clinical features of pulmonary edema in man, Welch concluded that relative left ventricular failure is the element *sine qua non* for the development of pulmonary edema. Actually, there is much in clinical experience to justify his conclusion. It is well known, for instance, that patients with heart disease and distressing attacks of pulmonary edema are frequently relieved when right-sided failure supervenes. Right-sided failure tends to lower pulmonary artery pressure, which is reported to be abnormally high[7,10] in patients who have attacks of pulmonary edema, and thus relieves congestion in the pulmonary circuit.

In addition to the factors of increased pulmonary artery pressure and relative stasis in the pulmonary circulation, many have stressed the importance of anoxia leading to capillary damage and resultant increased permeability of the vessels as an aggravant to pulmonary edema.

But, while the clinician is led to seek a primary cardiac mechanism in pulmonary edema in a very great proportion of his cases, he will occasionally come across patients who show no overt signs of cardiac failure, who do not have the characteristic symptoms of pulmonary edema and yet who do have striking roentgen changes and prove to have pulmonary edema at autopsy. A significant number of these clinically atypical patients are in uremia; some of them have had central nervous system lesions, and some have been exposed to poisonous fumes.

In none of these instances, of course, can it be said with confidence that the patient has absolutely normal cardiac function. We can only ascertain that the electrocardiogram is normal, that the heart is not enlarged, that it is essentially normal to auscultation, and that there are no peripheral signs of failure. Thus far, then, the mechanisms by which pulmonary edema is produced remain, to some extent, a matter of speculation.

Fig. 1. Central pulmonary edema. Glomerulonephritis.

It is common knowledge that renal azotemic patients often have a hemorrhagic tendency, very likely due to vascular damage; pulmonary edema could develop on such a basis. Since there is almost always hypertension in uremia, it is particularly difficult to rule out the element of cardiac failure in this group.

There is little doubt that central nervous system stimuli can produce massive pulmonary edema in animals,[11] and one must suspect from a review of actual cases that the same is true in man. Three of our cases had central nervous system lesions only: one had had a hemispherectomy for brain tumor, and the other two, one of whom died, had subarachnoid bleeding. Many will think of patients with rheumatic heart disease in their own experience who have evidently been thrown into an attack of pulmonary edema by an emotional shock. One is led to speculate in these cases on the similarity between a sudden vast stimulus to the sympathetic nervous system and injection of epinephrine, the latter being ca-

pable of eliciting overwhelming pulmonary edema in animals (probably by causing increased peripheral resistance and left ventricular failure). One of our patients showing massive central pulmonary edema had a pheochromocytoma.

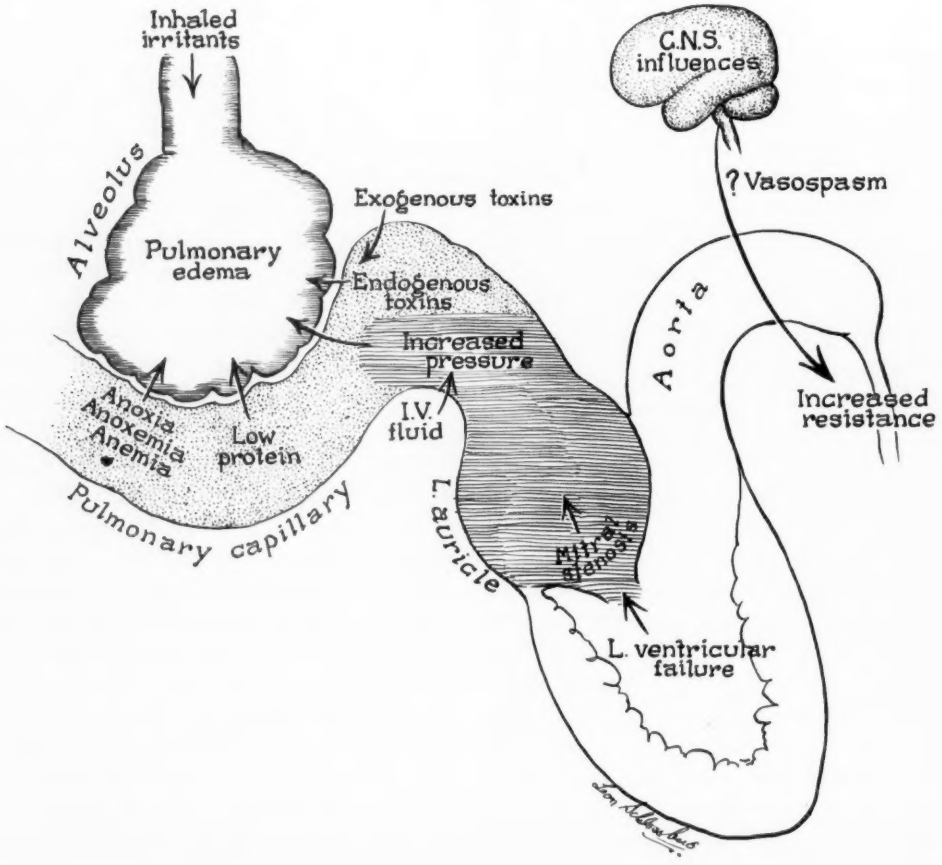
When we try to draw some conclusions about the pathogenesis of pulmonary edema on the basis of experiment and clinical observation, recognizing that increased capillary permeability is the immediate antecedent change, we find the following conditions of importance: (1) left ventricular failure; (2) anoxia causing capillary damage; (3) presence of some toxic substances causing capillary damage,[9] and (4) central nervous system stimuli operating through pathways not yet understood.[1]

How much each of these enters into a given case of pulmonary edema, especially with regard to left ventricular failure, is often impossible to determine (see diagram).

DEFINITION

Roentgenologically, pulmonary edema manifests itself by clouding or opacification of the lungs due to accumulation of fluid in the alveoli. The roentgen pattern of pulmonary edema must be differentiated from congestive changes and also dilatation of the pulmonary arteries and veins. The pulmonary vessels are enlarged and dilated with any process which significantly increases the blood pressure or blood flow in the lesser circulation. These dilated and enlarged vessels are noted in

DIAGRAM OF FACTORS IN FORMATION OF PULMONARY EDEMA



such conditions as mitral stenosis and insufficiency, cor pulmonale, Eisenmenger's syndrome, Lutembacher's syndrome, septal defects and patent ductus arteriosus, among other conditions. If the vessels are simply enlarged, they are sharp and clear. In congestive changes due to left ventricular failure, the vessels are both enlarged and hazy in outline. Presumably there is interstitial edema present, and perhaps very small collections of alveolar fluid which are not clearly distinguishable on the roentgenogram. There is no sharp line of demarcation between severe congestive changes and minimal pulmonary edema. Venous dilatation, congestion and pulmonary edema form a spectrum of pulmonary patterns which can change imperceptibly from one phase to the other. In our study we consider as congestive those changes which are characterized by enlarged blood vessels with hazy outlines. Frank edema is characterized by definite clouding or opacification of the lungs due to the accumulation of fluid in the alveoli. In frank edema the opacification or consolidation completely obliterates the vessels traversing the edematous portion of lung, since no contrast exists between the fluid-filled vessel and the fluid-filled alveoli. Because the alveoli are filled with fluid, the bronchi which traverse this portion of the edematous lung are revealed as radiolucent linear aborizations, since to the roentgen ray, contrast exists between the fluid-filled alveoli and the air-containing bronchi. Perhaps arbitrarily, therefore, we have relegated congestive changes to enlarged and hazy vessels in the lung, and pulmonary edema to a clouding or opacification of the lungs with obliteration of the vascular shadows and with the demonstration of small bronchial air shadows.

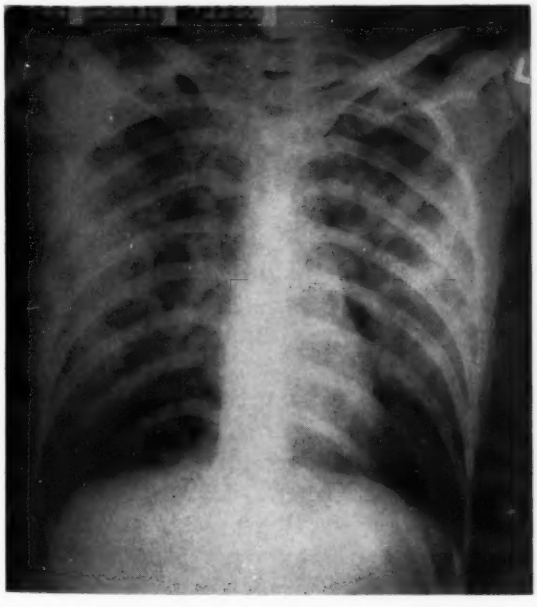


Fig. 2. Diffuse pulmonary edema. Transfusion reaction.

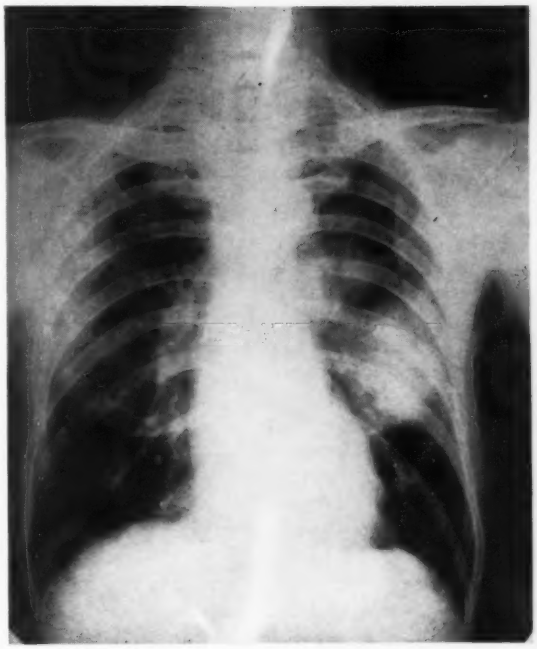


Fig. 3. Focal pulmonary edema. Multiple myeloma and uremia. Masses disappeared on medical management.

Because we have been unable to find in the literature any roentgenographic-morphologic classification of pulmonary edema,[15] we have devised the following working classification:

MORPHOLOGIC CLASSIFICATION OF PULMONARY EDEMA

Type I Central edema: Large, confluent or even homogeneous, dense, central or perihilar opaque shadows usually forming symmetrically bilateral densities, giv-

TABLE I

ETIOLOGIES IN 100 CASES OF PULMONARY EDEMA

Etiology	Total No. and Per Cent of Pulmonary Edema Cases
Rheumatic	22
Coronary	8
Bacterial endocarditis	2
Other cardiac	32
"Pure" uremic	13
"Complicated" uremic	12
Anemia	4
Central nervous system	3
Pulmonary infection	2
Pheochromocytoma	1
Transfusion reaction	1
TOTAL	100

ing the so-called "butterfly" or "bat's wing" appearance (Fig. 1).

Type II Diffuse edema: Patchy, ill-defined, usually bilateral densities, variable in size, and distributed in a diffuse fashion. These shadows are frequently of varying density (Fig. 2).

Type III Focal edema:

a) Lobar: dense, homogeneous consolidation bounded by a major fissure or fissures, predominantly lobar in distribution.

b) "Pseudosarcoma": one or more isolated, large, rounded, discrete shadows resembling primary or metastatic tumor (Fig. 3).

It may occur to the reader that there would logically be a "mixed" category in which the films would show a combination of the central and the diffuse types. This combination does occur, but in this series we have found that the central element appears to predominate, and these cases were, therefore, placed in the "central" classification.

STUDY

Our study consists of 100 cases of pulmonary edema abstracted from a total number of 982 patients considered to have entities which are known to produce episodes of pulmonary edema. These entities included clinical cases of bacterial endocarditis, hypertensive heart disease, rheumatic heart disease, syphilitic heart disease, coronary thrombosis, nephritides and pneumonias.[6] In addition, there were isolated interesting cases found among transfusion reactions, pheochromocytoma, carbon tetrachloride poisoning and multiple myeloma with uremia. In our series there were no cases due to the inhalation or aspiration of toxic pulmonary irritants. The gross proportion of pulmonary edema cases from our material is approximately 10 per cent. In comparing the incidence of pulmonary edema in uremic cases with that in cardiac patients without uremia, it was found that approximately 7 per cent of the uremic patients had pulmonary edema roentgenologically and 12 per cent of the cardiac group had pulmonary edema.

The 100 cases of pulmonary edema are divided into three main categories according to the morphologic features described in the foregoing classification: 90 central edema, 7 diffuse edema, and 3 focal edema. Table I is a breakdown according to etiology.

Since the central type of pulmonary edema is so preponderant, it was thought advisable to analyze this group further and subclassify it morphologically. Table II represents the morphologic breakdown according to 4 factors: definition, pattern, density and the presence or absence of congestion. Each film was graded from 1 to 4 plus for the groupings density and congestion. A density or congestion of 2 plus or greater put the case in the positive column.

It will be noted that the uremic cases which include the so-called "pure" uremic (those due to primary renal disease) and the "complicated" uremic (those in which renal failure was secondary to some other disease, most often advanced essential hypertension) tend to show a well defined and dense type of central edema without associated congestion.

On the other hand, the cardiac cases without uremia tend to show poorly de-

TABLE II

ROENTGENOLOGIC DESCRIPTION OF CENTRAL PULMONARY EDEMA

Group Category	Definition		Pattern		Density		Congestion		Group Total
	Well defined	Poorly defined	Nodular	Homogeneous	Dense	Not dense	Present	Absent	
Other cardiac	7	21	18	10	12	16	21	7	28
Rheumatic heart disease	4	17	11	10	10	11	18	3	21
"Pure" uremic	10	3	8	5	12	1	1	12	13
"Uncomplicated" uremic	9	1	8	2	8	2	2	8	10
Coronary thrombosis	2	5	2	5	6	1	4	3	7
Central nervous system	1	2	3	0	2	1	0	3	3
Anemia	0	3	1	2	1	2	1	2	3
Bacterial endocarditis	2	0	1	1	2	0	1	1	2
Bronchopneumonia	2	0	0	2	2	0	0	2	2
Pheochromocytoma	1	0	1	0	1	0	0	1	1
Category total	38	52	53	37	56	34	50	40	90

fined central edema of lower density and associated with congestive changes. The table shows considerable overlap, however, between the various classes, and there is no feature or combination of features which will consistently differentiate the so-called "uremic" pulmonary edema, for example, from that associated with cardiac failure alone[3] (*cf.* Fig. 4 and 8; Fig. 5 and 7).

Some of the patients who showed very dense, mass-like shadows and who came to necropsy had, in addition to alveolar edema, numerous areas in which the alveoli were filled with fibrin and macrophages.[2] This combination of findings suggests something less labile than serous pulmonary edema, and has led us to suppose that edematous zones may undergo fibrin coagulation and give rise to what has sometimes been called "uremic pneumonia" or "rheumatic pneumonia."[8] From the descriptions, the microscopic pictures are similar, whether the patient had uremia, rheumatic heart disease, or an undetected myocardial infarct. Thus, we suspect that an area of chronic edema may undergo a "pneumonic" or "consolidative" change, regardless of the cause of edema.

The roentgen diagnosis of massive pulmonary edema carries with it a poor prognosis. The great majority of such cases in our series died within several days or weeks.

The fact that 90 per cent of all our edema cases have been central has given rise to considerable speculation as to the cause of this localization. Is this central localization due to the summation of shadows in the thickest portion of the lung? We believe it is not, because the line of demarcation between the central edematous and peripheral clear portions of the lung is often too sharp to be explained by a simple volume fall-off. The most cogent explanation for this phenomenon seems to us to be the relatively greater excursion of the peripheral lung (including the portion just above the diaphragm), which gives rise to a squeezing or bellows-like effect most pronounced immediately beneath the chest wall. This pumping action would encourage the re-

TABLE III

ROENTGENOLOGIC SUBCLASSIFICATION OF CENTRAL PULMONARY EDEMA

Category	Massive	Mixed	Congestive	Disease Total
Other cardiac	2	3	23	28
Rheumatic heart disease	3	5	13	21
"Pure" uremic	8	3	2	13
"Uncomplicated" uremic	6	4	0	10
Coronary thrombosis	2	2	3	7
Central nervous system	1	2	0	3
Anemia	1	1	1	3
Bacterial endocarditis	1	1	0	2
Bronchopneumonia	1	1	0	2
Pheochromocytoma	0	1	0	1
Category total	25	23	42	90

moval of lymph and fluid which may accumulate in the periphery.

From the experience gained from the collection of data for Table II a subclassification of central pulmonary edema suggests itself. The cases seem to fall into three groupings, which, for want of more descriptiv titles, we are terming "massive," "congestive" and "mixed" (Fig. 4, 5, and 6). By "massive" is meant rather discrete, dense and usually extensive central edema. By "congestive" we mean central edema which is poorly defined, less dense and showing a well developed pattern of superimposed congestion. Cases in the "mixed" category show massive central edema as well as congestion. Table III is a breakdown of our experience according to this

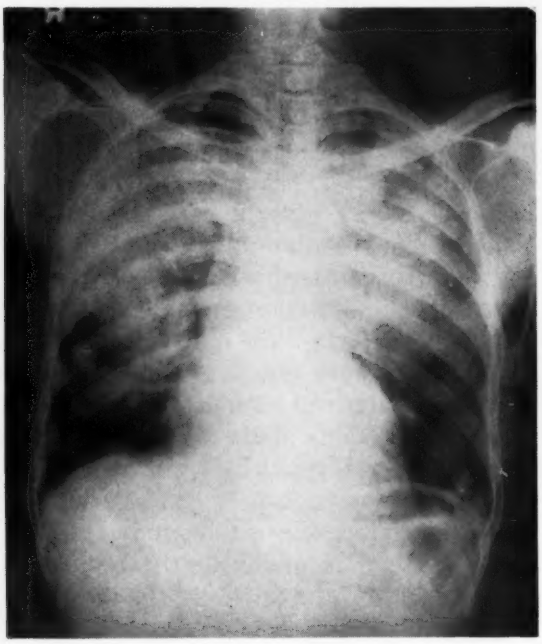


FIG. 4. Massive central pulmonary edema. Glomerulonephritis in uremia. Note similarity to Figure 7, a "pure" cardiac.

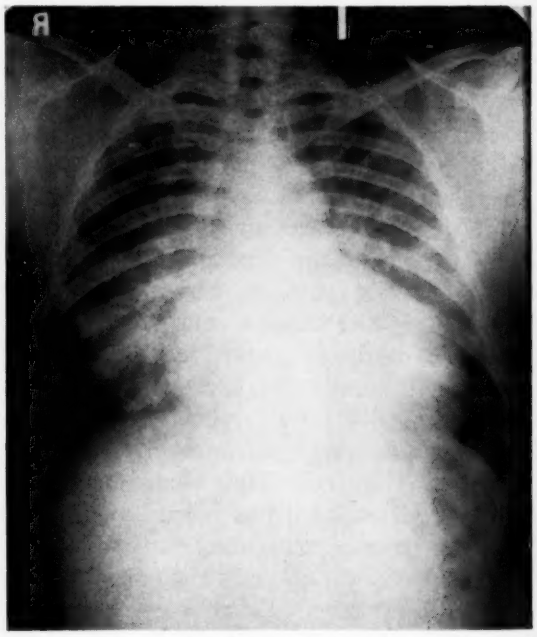


FIG. 5. Congestive central pulmonary edema. Rheumatic heart disease with aortic insufficiency. Compare with Figure 8, which also shows a predominantly congestive pattern, even though the patient is in uremia.

subclassification (Fig. 7 and 8). The entire series contains 7 cases in the "diffuse" class. The breakdown on these is as follows: 1 rheumatic myocarditis, 3 other cardiac, 1 coronary occlusion, 1 sickle cell anemia in crisis, and 1 transfusion reaction. It is of clinical interest that each of these cases can be considered in acute pulmonary edema at the time of roentgen examination.

Cases of focal edema proved rare, our series containing only 3: 1 case of multiple myeloma in uremia and 2 cases of complicated uremia. In the 2 cases of complicated uremia serial roentgenograms showed varying patterns. The edema first appeared as a lobar type and later became a fairly typical massive central edema.

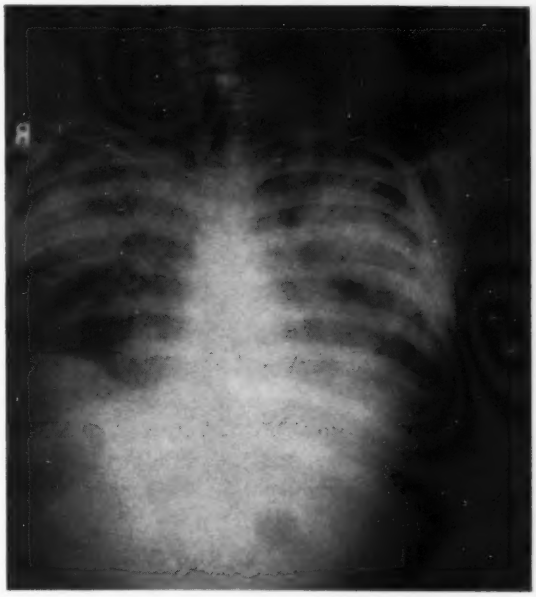


Fig. 7. Massive central pulmonary edema without uremia. Rheumatic heart disease. Note dissimilarity to Figure 5 even though both patients are cardiacs without uremia.

DIFFERENTIAL DIAGNOSIS

It was striking in our series how often pulmonary edema was confused with pulmonary infarction or bronchopneumonia. Pulmonary infarction appears to be quite a logical diagnosis because of the signs of congestive failure, enlarged heart and hemoptysis. A point in favor of pulmonary edema is the absence of pleural pain. Of course, the two conditions, pulmonary edema and infarction, often coexist.

When the patient has a fever and leu-

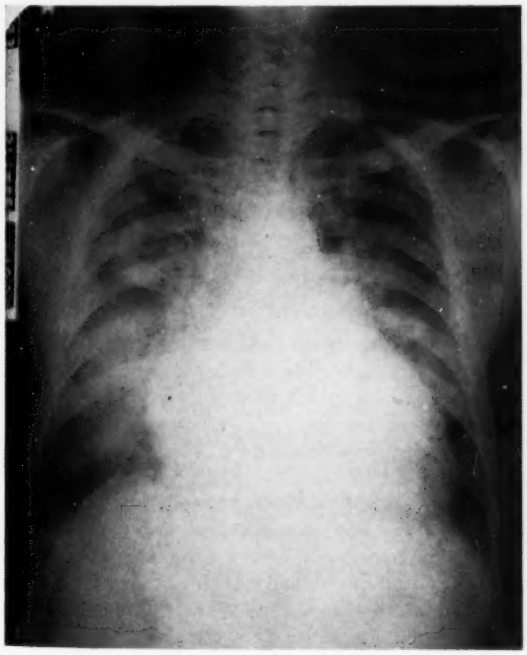


Fig. 6. Mixed central pulmonary edema. Rheumatic heart disease with aortic and mitral stenosis and insufficiency. The original roentgenogram showed fairly discrete central edema on the right side.

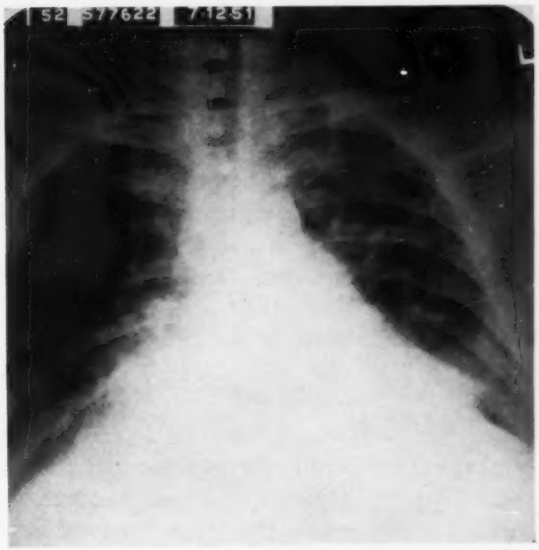


Fig. 8. Central congestive pulmonary edema with uremia. Hypertensive heart disease. Note dissimilarity to Figure 4 even though both patients are uremic.

kocytosis, bronchopneumonia suggests itself. Indeed, it is difficult to ascribe a high fever and signs of infection to pulmonary edema alone. Both clinical and necropsy evidence points to the conclusion that pulmonary edema is often complicated by bronchopneumonia, or vice versa. No doubt in a patient who is on the precarious edge of compensation, a respiratory infection or any type of infection, by putting more demand on the cardiovascular system, may tip the balance in favor of pulmonary edema.

Particularly in nephritic cases, the diagnosis of gastrointestinal malignancy is entertained. The evidence such as nausea, vomiting, weight loss, anorexia, anemia and gastrointestinal bleeding makes an excellent case for malignancy.

The rare type of focal edema which produces a spherical mass in the lung often strikes both the clinician and radiologist as a lung tumor, either primary or metastatic. Indeed, one of our cases traveled halfway around the world for a lung operation, only to have the mass disappear on medical management (Fig. 3).

From a roentgen viewpoint we have noticed frequent cases of pulmonary edema which were first diagnosed as pulmonary tuberculosis, pneumoconiosis, sarcoid, infarct and bronchopneumonia. Conversely, in our experience it has been rare to find a case of misdiagnosed pulmonary edema that was actually another entity. The only two cases we discovered were one of sarcoid and one of tuberculosis, and there was some doubt in the latter case as to whether there was indeed an element of edema complicating the proven tuberculous infection.

SUMMARY

1. One hundred cases of pulmonary edema are analyzed morphologically.

2. This series shows no single distinctive pattern differentiating the underlying causes of pulmonary edema.

3. There is some correlation between the massive central type of edema without congestive changes and uremia.

4. There is some correlation between the poorly defined congestive type of edema and cardiac failure without uremia.

5. A roentgen pattern characteristic of pulmonary edema is not necessarily associated with the clinical signs usually ascribed to pulmonary edema.

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LOBAR EMPHYSEMA*

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THE clinical and pathological findings in lobar emphysema have been discussed by authors in the pediatric,[5,6,11,19,21,23,25] medical,[2,3,14,17,24] and surgical literature.[1,13,15,16,22,26,29] Whereas, the roentgenological literature[9,10] describes the entity, we feel that insufficient emphasis has been placed on the correlation between the clinical symptoms and signs, and the roentgenographic appearance. The central nervous system complications of hypoxia due to this pathologic entity have been largely ignored. These may be so severe in spite of early diagnosis and surgical treatment that irreparable changes occur. It is well known that hypoxia, even of short duration, is poorly tolerated in infants and children and can produce neurologically demonstrable central nervous system damage. Since the diagnosis is made by radiologists, we felt that it was worth while to chronicle our difficulties not only in diagnosis, but in the insistence of early surgical attack for this severe respiratory emergency in infants.

Two cases of lobar emphysema are being reported.‡ The clinical findings are included in this report because we feel that, although a clear understanding of the sequence of events is important in helping to make the diagnosis, they are not pathognomonic. To illustrate a case in point, we are also presenting a somewhat older infant with cystic disease of the lung. In all 3 cases the correct diagnosis was made, although considerable doubt existed in our minds as well as in those of our pediatric and surgical confrères as to the significance of the initial roentgenoscopic and roentgenographic examination in our first patient.

CASE 1. N.W., female, born February 17, 1952, was admitted to the University Hospitals at twelve days of age with the complaint of shortness of breath and cyanosis. A significant finding in the family history was that a previous child had died suddenly in her sleep at the age of two weeks. The thymus was implicated as a causative factor in this sudden death.

The baby was full term and weighed 8 pounds and 6 ounces. She cried spontaneously. No respiratory difficulty was noted at birth nor in the first twenty-four hours. On the second day it was noted that the baby was cyanotic and was not using the left side of the chest on respiration. Respirations were grunting. The child was placed in oxygen and kept there continuously, since, when she was taken out even for a few minutes, she became cyanotic.

The local physician made a diagnosis of agenesis of the left lung. This was based on the clinical and roentgenographic findings.

On admission to University Hospitals the child was in severe respiratory distress, having pronounced substernal retraction. Cyanosis about the lips was present. This became more intense when the child was taken out of oxygen. Physical examination revealed hyperresonance on the right. The thorax appeared emphysematous. Breath sounds were heard on both sides but better on the left side posteriorly. No significant tracheal displacement was found. The heart, however, was displaced to the left. The clinical impression was: malformation of the lung, agenesis, left, or cystic disease. There was no fever and all laboratory studies were normal.

Roentgenoscopic examination was done on the day after admission. This revealed depression of the diaphragm on each side with poor movements bilaterally. The rapid, shallow respirations did not produce any mediastinal shift such as one would expect to see in obstructive emphysema. There was, however, a fixed shift of the heart and mediastinum to the left with herniation of the right middle lobe anteriorly across the midline, deviating the trachea

‡ Surgical aspects of these cases are published by J. L. Ehrenhaft and R. E. Taber, Department of Surgery, University Hospitals, Iowa City, Iowa. (*Surgery*, Sept., 1953, *34*, 412–425.)

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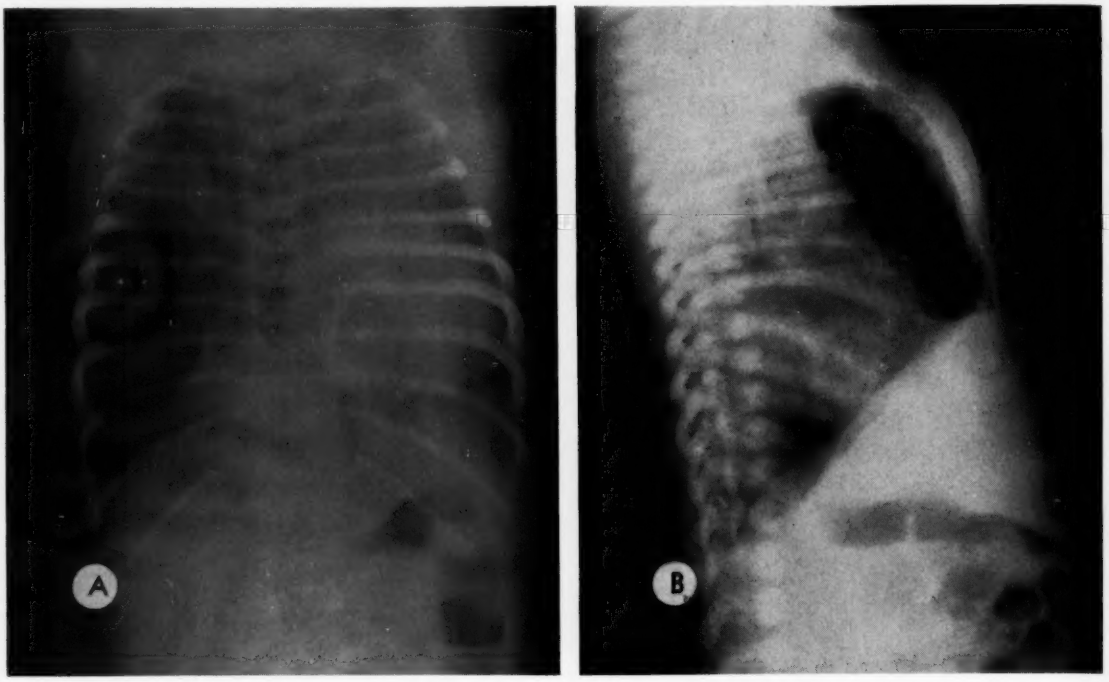

Fig. 1. Case 1. (*A*) Posteroanterior and (*B*) right lateral films of the chest. The increased density of the upper lobes and the right lower lobe is due to the compression by the extremely emphysematous middle lobe. Displacement of the heart and mediastinum to the left with only posterior displacement of the trachea is also due to the increased size of the middle lobe. Diaphragmatic depression is moderate.

posteriorly. The right upper and lower lobes showed diminished volume with emphysema in the right midlung field. Figure 1 demonstrates the changes seen roentgenoscopically. Note the emphysematous middle lobe, the compression of the upper and lower lobes on the right and of the upper lobe on the left, the displacement of the heart and mediastinum to the left, the herniation of the middle lobe anteriorly across the midline displacing the trachea posteriorly, but not to the left, and the distorted vascular pattern in the middle lobe.

Our first impression was that the compressed upper lobes were the sites of a pneumonic process. Because of the distorted vascular pattern in the middle lobe, cystic disease of the lung was suspected. Since all of us felt that the changes were bilateral, no surgical attack was considered to be feasible.

Repeat roentgenograms were requested, but not obtained for three intervening days. They are shown in Figures 2 and 3. There is a significant increase in the degree of emphysema of the middle lobe. Associated with the roentgenographic change was a clinical deterioration of the patient which occurred in the interval between the taking of the two lateral films. It was at this time that the true process was appreciated and the diagnosis made. Immediate operation was advised.

Anesthesia was difficult, but upon opening the chest, respirations suddenly improved. Bulging into the thoracotomy wound was the extremely emphysematous middle lobe which compressed the upper and lower lobes. The middle lobe extended across the midline through the anterior mediastinum into the left hemithorax. A right middle lobe lobectomy was done. The upper and lower lobes were expanded and immediately filled the right hemithorax. At the conclusion of the operation the child breathed normally and without visible cyanosis being present.

Pathological examination of the removed middle lobe revealed it to be enlarged measuring 9 by 5 cm. in size. No cysts were seen. There was no evidence of proliferation of embryonic lung tissue. Microscopic examinations (a representative slide is shown in Fig. 4) revealed normal large bronchi with normal cartilage plates. The alveoli in places were atelectatic, but generally considerably dilated and lined

by flattened cells. The pathologic impression was: enlarged right middle lobe, with lipoid pneumonia, mild.

Follow-up studies were done with the last examination occurring on April 17, 1953, at the age of fourteen months. No abnormalities were noted. The patient's growth and development were normal. The last chest film taken on that date is shown in Figure 5.

Comment. Erroneous diagnoses in this case are quite illustrative and compare with those made in previously reported cases. They included agenesis, and/or cystic disease of the *left* lung, bilateral pneumonitis with cystic disease of the right middle lobe, atelectasis of the upper lobes and compensatory emphysema of the lower and middle lobes. Because of these varied diagnoses, and because it was felt that bilateral disease was present, immediate surgery was felt to be contraindicated. Progress examination indicated the correct diagnosis and immediate surgery was life saving. In spite of the delay in surgery on this patient, and in spite of the severity of the symptoms, no signs have ever been detected to indicate any effect of cerebral anoxia.

Case II. J.McG., female born August 5, 1952, was admitted to the University Hospitals at seventeen days of age with the complaint of difficult respirations and cyanosis. She was a full term child. No family history of sudden death, or similar respiratory difficulties was elicited. This infant did quite well for the first five days of life, but at that time she became cyanotic, stopped nursing and refused to resume breast feeding. A roentgenogram was taken at fifteen days of age and interpreted as showing atelectasis of the left upper lobe (Fig. 6).

Physical examination at the time of admission revealed an acutely ill child with respiratory difficulty, cyanosis when out of oxygen, hyperresonant right hemithorax with diminished to absent breath sounds on this side, crepitant rales on the left, no cardiac abnormalities and no shift of the mediastinum. Laboratory studies were normal. There was no fever. The clinical impression was: pneumothorax, right.

Roentgenograms were obtained on admission, a few hours after the initial outside film, and twelve hours later. The latter films were

Fig. 2. Case I. Posteroanterior roentgenogram of the chest taken three days later. There is an increase in the amount of emphysema with progressive herniation of the middle lobe across the mediastinum anteriorly displacing the trachea posteriorly, but not to the left. As in the previous instance, the distorted vascular pattern is demonstrated within the middle lobe.

the first that we read. The series is shown in Figures 7 and 8. Note the emphysema of the right middle lobe with compression of the upper and lower lobes, the depression of the diaphragm, the herniation of the middle lobe anteriorly across the midline displacing the trachea posteriorly and the heart to the left, and the distortion of the vascular pattern in the middle lobe.

A diagnosis of lobar emphysema was made and immediate surgical removal of the middle lobe was advised. Within one hour the patient was undergoing this procedure. As in the previous case, anesthesia induction was precarious and difficult, but upon entering the chest, the respirations improved with the bulging of the emphysematous middle lobe into the thoracotomy wound. At surgery it was noted that there was collapse of the right upper and lower lobes. The entire right hemithorax was filled with the extremely emphysematous middle lobe. A right middle lobe lobectomy was done.

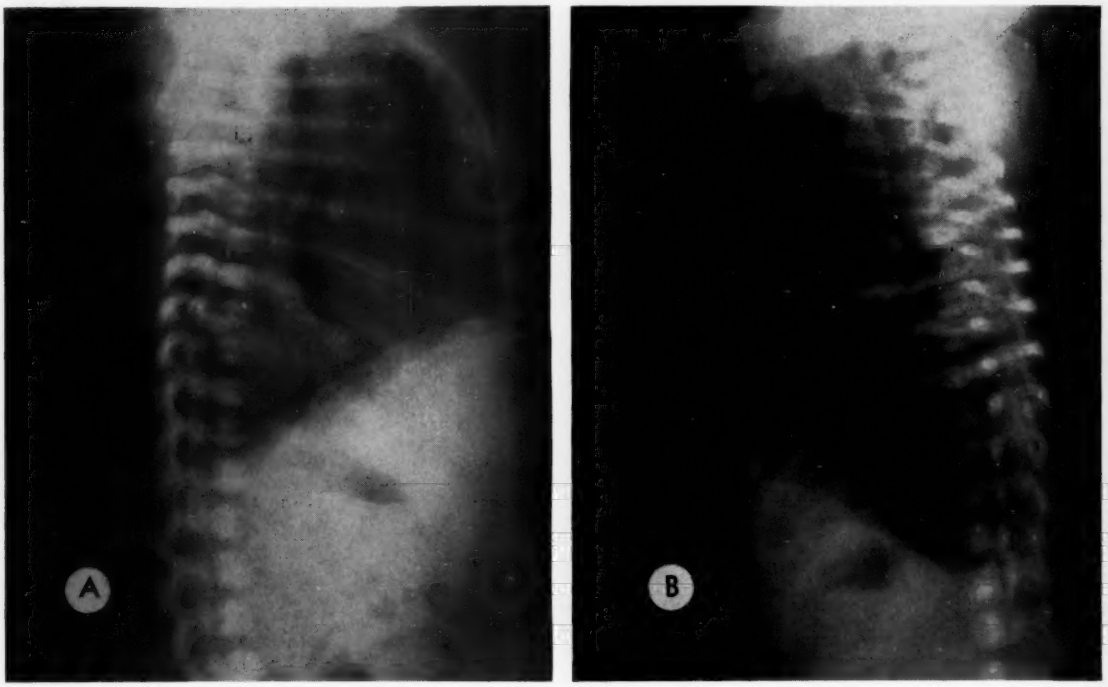

Fig. 3. Case 1. (*A*) Right and (*B*) left lateral films of the chest. These were obtained at the same time as the film in Figure 2. Note the difference in the degree of herniation of the middle lobe anteriorly across the midline. Clinically the change was manifested by an abrupt change for the worse in the child's respirations.

Pathological examination of the removed middle lobe revealed it to be enlarged, measuring 9 by 4.5 by 2 cm. in size. It floated in water. No cysts were seen. There was no evidence of proliferation of embryonic lung tissue. Microscopic examination (a representative slide is shown in Fig. 9) revealed normal parenchyma, bronchi and pulmonary vessels. The bronchioles were distended, but had normal epithelium. There was generalized emphysema with small patchy areas of atelectasis. Many of the alveoli were distended and were lined by a thin sheet of flattened cells. The pathologic impression was: emphysema with areas of focal atelectasis, middle lobe, right lung.

Progress roentgenograms taken at three months of age are shown in Figure 10. Note that no evidence of emphysema remains. Both lungs are now symmetrically ventilated. This child has had four severe upper respiratory infections since the surgery with no lower respiratory tract involvement. The last roentgenogram was taken in August, 1953. It is normal.

Comment. Erroneous diagnoses in this instance included atelectasis of the left upper lobe, pneumothorax on the right, compensatory emphysema of the right lung, cystic disease of the right lung. Our previous experience with the case described above indicated the correct diagnosis. Im-

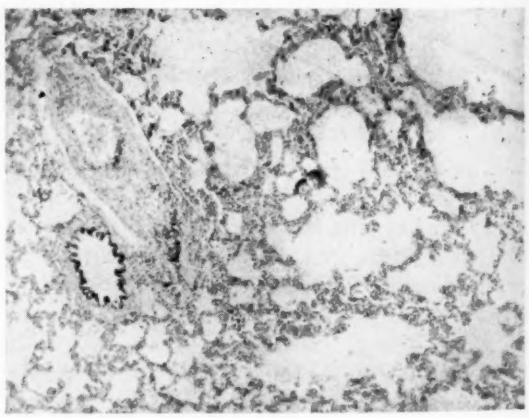

Fig. 4. Case 1. Photomicrograph showing a representative section of the surgically removed lobe. Note the focal atelectasis and the dilated alveoli which are lined by flattened cells. There is no evidence of cystic disease and no evidence of proliferation of embryonic lung tissue.

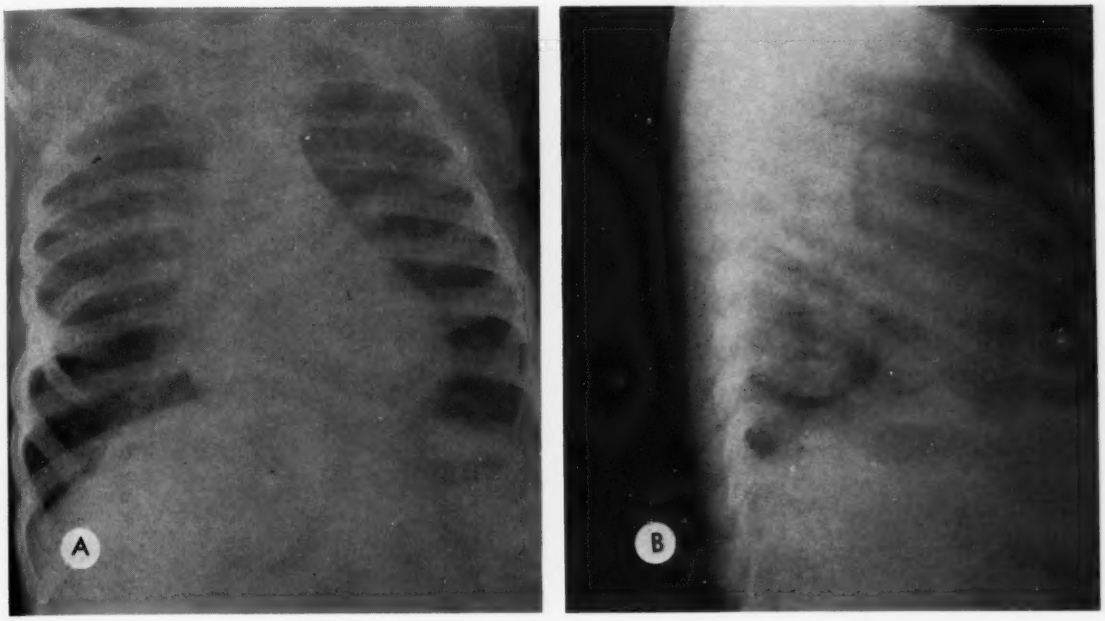

Fig. 5. Case I. (*A*) Posteroanterior and (*B*) right lateral films of the chest. Postoperative films at fourteen months of age demonstrating no abnormality of either lung field.

Fig. 6. Case II. Posteroanterior film of the chest taken prior to admission to University Hospitals. Note the emphysematous middle lobe compressing the upper and lower lobes on the right and the upper lobe on the left, and herniating anteriorly across the midline, shifting the heart and mediastinum to the left.

mediate surgery was advised and done.

In the twelve hours between the initial and the second roentgen examination, the child deteriorated considerably. She became cyanotic even while in oxygen and refused to nurse. Apprehension was felt for the development of cerebral anoxia. Follow-up examinations have been regularly carried out and have shown definite motor retardation with much less degree of mental retardation. No spasticity has developed. A guarded prognosis for future development has been given, although it is felt that she has given recent evidence of advance in both motor and mental achievements.

Case III. M. S., male was admitted to the University Hospitals at the age of five months on June 10, 1951, with the complaint of grunting respirations for the past two months, increasing in severity and degree on June 8, 1951, so that the child had to be held erect. No cyanosis was ever noted. Clinical examination revealed hyperresonance of the left hemithorax with diminished to absent breath sounds on this side. The heart and trachea were shifted to the right. There was anterior bowing of the

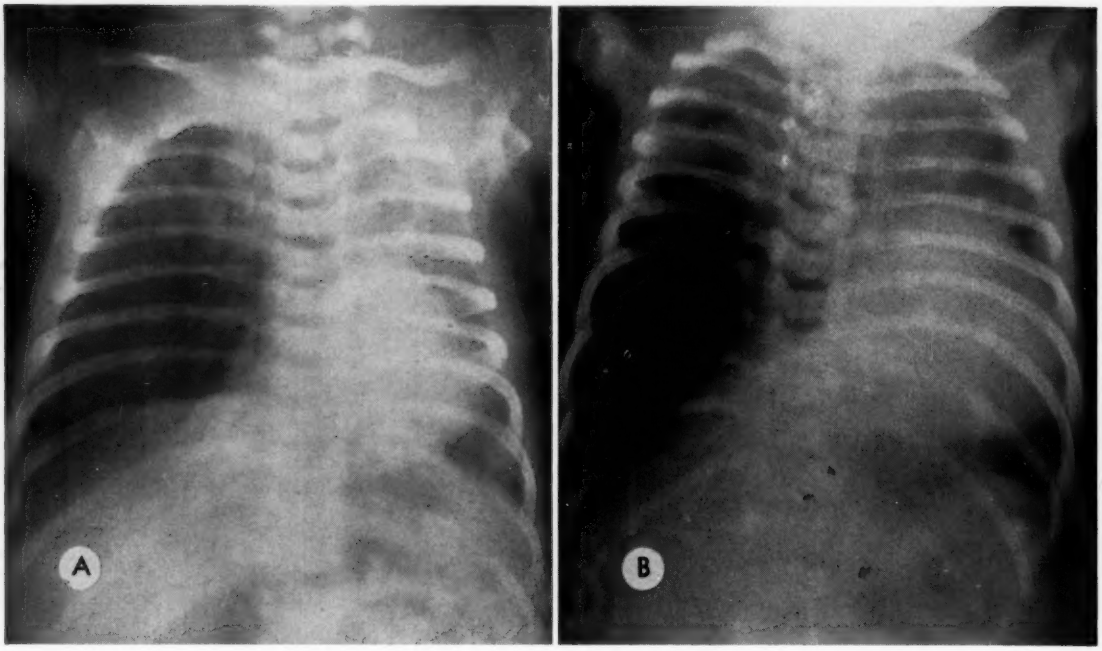

FIG. 7. Case II. (*A*) (*B*) Posteroanterior films of the chest with only a few minutes' interval between the exposures. Note the distorted vascular pattern in the extremely emphysematous middle lobe. This compresses the upper lobes bilaterally and the right lower lobe, and herniates across the midline into the left hemithorax. Diaphragmatic depression is evident.

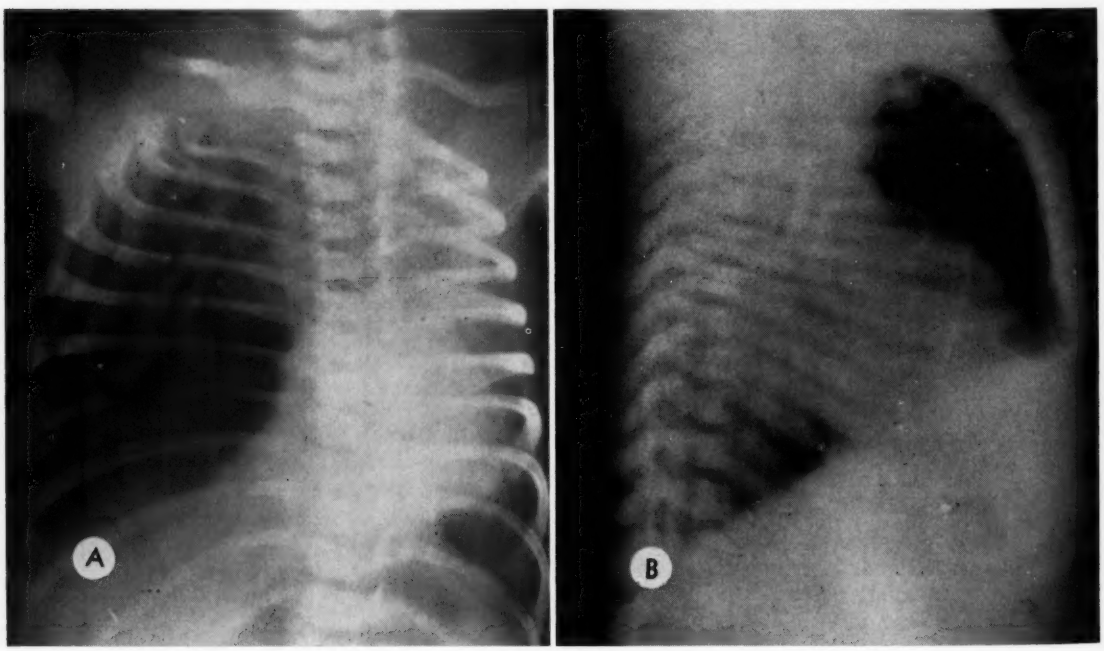

FIG. 8. Case II. (*A*) Posteroanterior and (*B*) right lateral films of the chest taken twelve hours after those shown in Figure 7. Clinically the child deteriorated considerably in the interim between the two sets of films. There has been little apparent progression of the roentgenographic findings.

sternum and retraction of the intercostal spaces along the diaphragmatic attachments. Laboratory studies were normal. There was no fever. The clinical impression was: tension pneumothorax, left.

Roentgenograms are shown in Figure 11. Note the emphysema of the left upper lobe, the herniation of the upper mediastinum anteriorly across the midline, the compression of the lower lobe, and the attenuation of the left main bronchus. The extreme radiolucency of the upper lobe and the thin, irregular septa suggested that large bullae or cysts were present and that diagnosis was indicated on our report. There was no evidence of a pneumothorax. The vascular pattern was invisible.

Because of increasing respiratory difficulty surgery was indicated and done one day after admission. Again difficulty was noted in the induction of anesthesia, but the embarrassed respirations became more regular and deeper when the thorax was opened. The left upper lobe bulged into the thoracotomy wound. Many cysts were seen within the left upper lobe. These cysts were confined, however, to the subapical, the anterior pectoral and axillary segments. The bronchus going to the anterior pectoral segment was found to be small and narrowed. Segmental resection of the involved lung was carried out.

Pathological examination of the removed lobe revealed no cysts grossly because the lung had been incised in several areas. Microscopically there was a normal subpleural parenchyma. In the deeper portions of the tissue large cystic areas lined with moderately tall columnar epithelium were noted. The cysts varied in size and many of them were filled with partially hemolyzed blood and pink-staining fluid. The pathologic impression was: cystic disease, left upper lobe. A representative section of this lobe is shown in Figure 12.

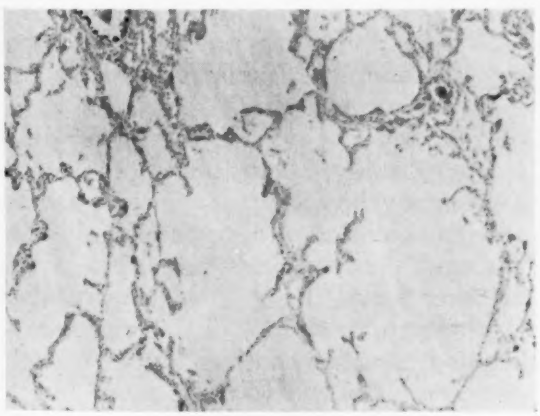

Fig. 9. Case 11. Photomicrograph showing a representative section of the surgically removed middle lobe. Note the degree of alveolar distention. This is much greater than that of Case 1. The distended alveoli are lined by a thin sheet of flattened cells. There is no evidence of cystic disease and no evidence of proliferation of embryonic lung tissue.

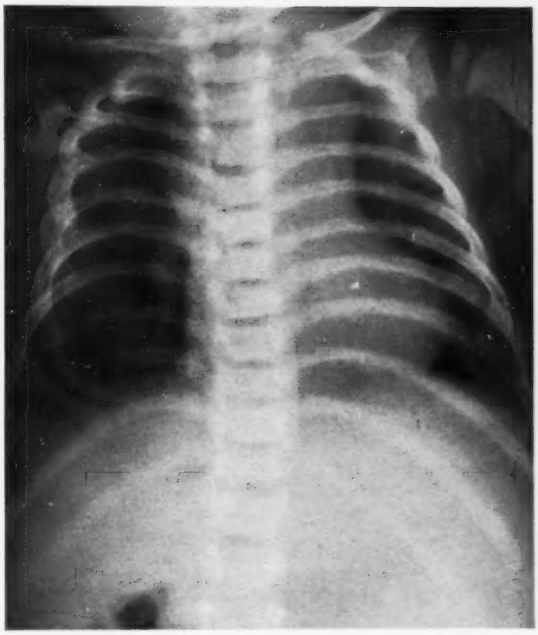

Fig. 10. Case 11. Posteroanterior film of the chest taken at the age of three months reveals a healthy postoperative chest. Aeration is equal and symmetrical. A film taken in September, 1953, at the age of thirteen months is also normal.

The last clinical and roentgenographic follow-up was on August 8, 1951, at which time the child was normal clinically. Although the films are lost, our report states that "aside from mild thickening of the pleura in the left base and slight deviation of the heart and mediastinal structures to the right, no abnormalities or evidence of recurrent cystic disease is present."

Comment. Clinically and roentgenographically the lesion in this patient was similar to that seen in the cases of lobar emphysema. Pathologically the lesions are different since in this case there are cysts with moderately tall columnar epithelium. The significance of the stenosed anterior

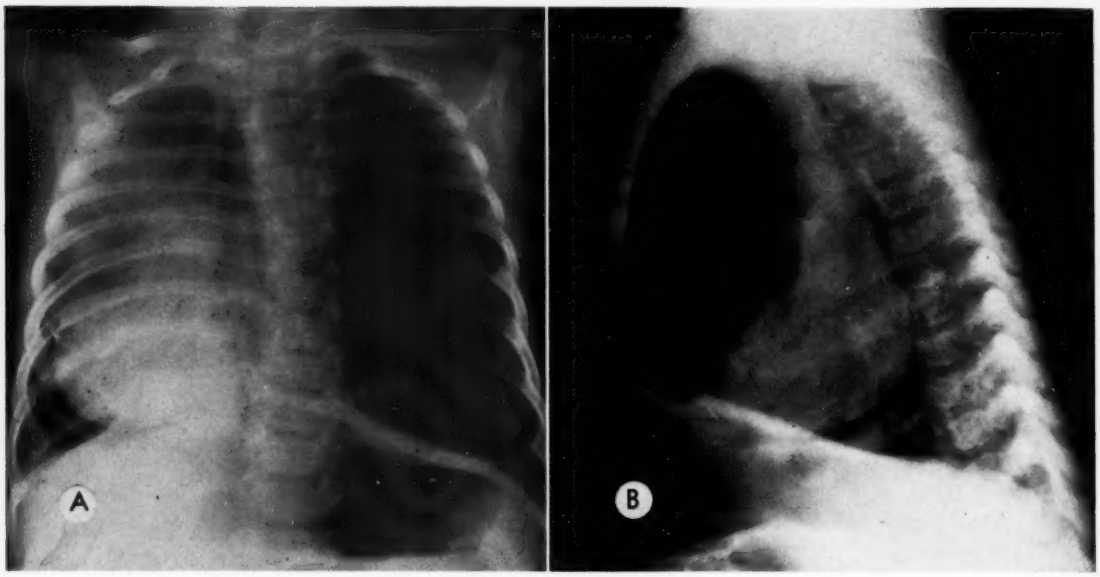

FIG. 11. Case III (*A*) Posteroanterior and (*B*) left lateral films of the chest. An interesting feature of these films is that the depression of the diaphragm is for the most part on the left side. There is deviation of the trachea to the right and posteriorly due to herniation of the left upper lobe through the anterior mediastinum. Attenuation of the left main bronchus is present. Compression of the lingula and lower lobe on the left is severe, but there is also compression of the right upper lobe as well. The heart is shifted to the right and posteriorly. On the original films several cysts or bullae were noted and for that reason cystic disease of the lung was suspected.

pectoral bronchus in the production of these cysts cannot be stated, although it seems doubtful to us that a narrowed bronchus alone would be able to produce the changes described above. The presence of cystic changes in the lobe plus the abnormal bronchus suggests that the changes are the result of a developmental anomaly.

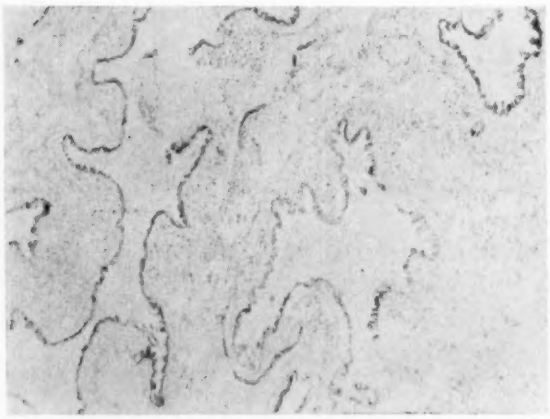

FIG. 12. Case III. Photomicrograph showing a representative section of the surgically removed lobe. Note the cysts lined with tall columnar epithelium.

However, it is difficult to believe that the roentgenographic picture is due solely to this anomaly or acquired abnormality. A more plausible explanation would be that, in addition to the anomaly, when present, there is an acquired component which varies in its ability to produce roentgenographic changes. If the abnormality is primarily a proximal check-valve mechanism, obstructive emphysema results. If it is located distally, segmental emphysema or a cyst may be seen roentgenographically. If a combination of abnormalities is present, multiple cystic changes may be noted. In other words, the physiologic response of the lung to an abnormality, congenital or acquired, must be considered.

DISCUSSION

Lobar emphysema is not only an entity but is also an acute respiratory emergency seen in infants and more rarely in children and adults. Clinically and roentgenographically it is an obstructive emphysema of varied etiology. The following causes have

been reported in the literature: redundant bronchial mucosa acting as a check-valve obstruction, deficiency in numbers or abnormal development of cartilaginous rings, compression by aberrant vessels such as the ductus or ligamentous arteriosus, stenosed bronchi, and trauma to the lungs incident to overstrenuous resuscitative measures at birth. There are also reported instances in the literature where no abnormality could be found. This was true in our 2 cases. Do the cases of unknown etiology manifest an abnormal physiological response based on some as yet undetected structural abnormality within the lung, or has the pathologist been unable to detect subtle changes either in the bronchi or parenchyma?

One of the cardinal features of this entity has been the finding of a uniformly pink overdistended lung which does not collapse upon removal. We postulated that perhaps some intrinsic abnormality of elastic tissue was a factor in its development. Special studies and extensive sectioning of the tissues made available to the pathologist neither confirm nor, as yet, deny this possibility. It is our plan in the next case to examine the entire removed lobe under positive and negative pressures in order to better understand the pathologic physiology of this condition. Further studies of elastic tissue will also be made.

The clinical and roentgenographic interpretation of the findings may be misleading. The clinical story usually follows a pattern: a previously normal infant begins to have attacks of dyspnea with or without cyanosis. These attacks become more severe and alarming, not only to the parents but also to the physician. Clinical examination reveals emphysema with decreased breath sounds, shift of the mediastinum and heart, and substernal retraction. Infection is not present. Atelectasis or pneumothorax is usually suspected.

Roentgenograms of the chest indicate the correct diagnosis. Extensive degree of emphysema is demonstrated, lobar in distribution, producing compression of the adjacent lobes, shift of the heart and mediastinum to the opposite side as well as posteriorly due to anterior herniation in the severe cases of the emphysematous lobe into the opposite hemithorax. The vascular pattern in the emphysematous lobe is distorted and separated, and not as irregular and thin as the septa seen in cystic disease of the lung. The diaphragm is flattened, depressed and never elevated.

The roentgen findings have been confused with pneumothorax, atelectasis of the opposite side, tension cysts, cystic disease, foreign bodies, diaphragmatic hernia, agenesis and bronchial plugging by thick viscid mucus in asthma and fibrocystic disease of the pancreas.

Since radiologists are usually the first to view the roentgenograms in these patients, they should be able to recognize the lesion. As with so many entities, the diagnosis is easily established if one not only thinks of the possibility of such a condition, but also recognizes and understands the underlying pathological process. As Caffey[6] has pointed out, the symptoms and signs are more alarming in these cases than in those with demonstrable cysts. It is these cases that frequently require immediate surgery. Caffey does, however, report 2 cases of lobar emphysema whose symptoms spontaneously disappeared and whose emphysema gradually decreased over many months. As in so many other lesions, variations in severity from case to case must be expected. The need for lobectomy will depend primarily on the clinical symptoms and findings; therefore, no generalization as to the best form of treatment should be made. The possibility of central nervous system damage from hypoxia must be taken into consideration by the clinicians in their evaluation of the patient for lobectomy.

Is cystic disease of the lung a congenital or an acquired lesion?[4,6,8,18,20,28] There are documented cases of congenital cystic disease. Many more cases of acquired cystic disease, however, are reported. We believe that congenital cystic disease should have

an associated anomaly of the lung in addition to the cystic change. The presence of columnar epithelium does not necessarily indicate the congenital nature of the lesion, since it has been shown experimentally by Condon[7] that respiratory epithelium, like epithelium elsewhere, is very responsive to injury. In young adult rats, Condon shows that trauma to tracheal epithelium has been repaired first by squamous epithelium in a few hours, and then in from three to ten days the epithelium has changed to ciliated columnar epithelium. Although there is no proof in human infants, it is likely that the phenomenon of injury and repair discussed above may occur. If this is true, then it is also likely that the presence of epithelial linings in pulmonary cysts or cystic disease is no index of the congenital nature of the process. The roentgenographic changes manifestly depend upon the response of the abnormal parenchyma to the normal forces of respiration. Whereas the production of solitary cysts is understandable, the mechanisms involved in the production of cystic disease is not. The possibility that it represents an injury and repair phenomenon should be considered.

The symptoms in this case were not as severe as in the 2 cases of lobar emphysema. However, an acute episode of respiratory distress necessitated a lobectomy. Roentgenographically the separated thin septa suggested that this was a case of cystic disease rather than lobar emphysema, with its distorted but typical vascular pattern.

The decision to surgically remove an abnormal lobe depends on the clinical response of the patient. When the symptoms of respiratory embarrassment are severe, surgery is indicated. If the symptoms are mild, a policy of watchful waiting should be adopted, since the life history of solitary cysts indicates that spontaneous recovery commonly occurs. The life history of diffuse cystic disease needs further study.

SUMMARY

1. Two cases of lobar emphysema have been reported. The clinical and roentgenographic findings have been emphasized. It is an acute respiratory emergency seen in infants and children, usually requiring immediate lobectomy for cure. Individual evaluation of the need for surgical correction must be made since spontaneous regression of symptoms and signs are known to occur.

2. Several types of check-valve obstructions have been reported to be the etiologic factor in some, but not all, cases. Absence of demonstrable abnormalities has been reported. Such was true in our two cases. Infection apparently does not play a part in the production of this lesion. Further studies are recommended to understand the pathologic physiology of this entity.

3. One case of cystic disease of the lung is also presented. Its similarity both clinically and roentgenologically to lobar emphysema is discussed. A brief discussion of the pathogenesis of pulmonary cysts and cystic disease is given.

4. Postmortem films should be taken in all cases of sudden death in infants in order to determine the frequency of lobar emphysema.

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The authors wish to make the following acknowledgments: Dr. L. C. Pumphrey, Keokuk, Iowa for the initial and follow-up films on Case 11; Dr. F. W. Stamler, Department of Pathology, for the studies on elastic tissue of the specimens of lobar emphysema.

ADDENDUM

Since the above cases were presented an additional case of lobar emphysema has been seen at the University Hospitals. A summary of the pertinent findings is herewith appended.

J. K. P., male, aged four and a half months when first seen at this hospital. At the age of six weeks he first began to have respiratory difficulty consisting of wheezing which progressively became more severe and for which three roentgen treatments to the thymus were given without any benefit. One of us (V. E.) interpreted films taken elsewhere as showing lobar emphysema of the right middle lobe and urged

that the child be sent in immediately to the hospital. Two weeks later the child was seen here in acute respiratory distress. Chest films again showed the same findings as presented in the 2 cases discussed above. It was interesting to find that the difficulties in diagnosis by the uninitiated encompassed the same differential diagnoses discussed above, and it was not until one of us who had seen previous cases made the correct diagnosis. The child was operated upon the same day and he, too, had severe respiratory difficulty during the induction of anesthesia.

A huge middle lobe measuring 12 by 8 by 6 cm. bulged out through the thoracotomy wound, immediately improving the child's respiration.

There were no abnormalities of the bronchi and no evidence of abnormality in the elastic tissue to account for this emphysema. The histopathologic pattern was exactly the same as described above for the other 2 cases.

The child did poorly following surgery because of the cerebral anoxia and also because of an associated congenital heart disease, the latter presumably being an interatrial septal defect.

The child was re-examined one month following surgery, but at this time there was no evidence of lobar emphysema. For the first time a systolic heart murmur was noted. One month later the child was reported to have died at home. No autopsy was done.

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DISCUSSION

Dr. E. B. D. Neuhauser, Boston, Massachusetts. Drs. Van Epps and Davies have entered into a field of discussion that we do not know too much about. They have entered courageously into a field where ideology is obscure, histopathology unclarified, but where by roentgen means we can give a very good idea of the mechanics and disturbed physiology.

I do not believe that Dr. Van Epps stressed sufficiently the danger of hypoxia in an infant. It may lead in even a few days to severe damage to the brain in a small infant. Prompt recognition and suitable treatment of these lesions that so grossly disturb the physiology of the lungs with resulting respiratory embarrassment and cerebral hypoxia is certainly necessary.

Vol. 73, No. 3

COMPARISON OF ESOPHAGOSCOPIC AND ROENTGENOLOGIC DIAGNOSIS OF ESOPHAGEAL VARICES IN CIRRHOSIS OF THE LIVER*

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THE diagnosis of esophageal varices can be made clinically by two methods. The most commonly used method of diagnosis is roentgen study of the esophagus with a barium meal. A more direct approach is visualization of the varices by esophagoscopy. The latter method has not been used as frequently as roentgen diagnosis, probably because of the ease of performance and lack of discomfort for the patient of roentgen diagnosis. However, the comparative reliability of diagnosis of varices by the two methods has not been previously reported as far as we can ascertain.

The diagnostic accuracy of the presence of esophageal varices becomes extremely important, especially in cases of gastrointestinal hemorrhage and in cases of portal cirrhosis of the liver, the most frequent condition in which varices are found. The clinical implications as to prognosis and treatment in the presence of varices, with or without a history of gastrointestinal bleeding, become even more pertinent since surgical methods to reduce portal hypertension seem successful in some instances. It appears to the authors that a method of diagnosis for reliable clinical examination not only should be without harm to the patient but should be dependable enough to ascertain the presence of varices before the catastrophic complication of hemorrhage occurs.

The accuracy of the roentgen diagnosis of esophageal varices has not been studied extensively. There are apparent differences of opinion on this subject among radiologists. While Ritvo and Shauffer[3] stated that the roentgen diagnosis of esophageal varices was so definitely established that it was now possible to recognize the lesion without the need of resorting to esophagoscopy, Zaino,[5] in presenting mineral oil contrast study to improve roentgen diagnosis of esophageal varices, reported figures, from various authors, varying from 15 to 50 per cent in demonstrating proved varices roentgenologically. A small but intensively studied series of cases of esophageal varices was reported by Hare, Silveus and Ruoff.[2] These authors studied 16 patients with cirrhosis of the liver, in which varices of the esophagus were demonstrated at autopsy in nine. Twelve of the 16 had roentgen study and varices were demonstrated in only 2 instances, in 1 of which the varices were not present at postmortem examination. In this small series, varices were present at death in about 50 per cent of cases, but could only be shown by roentgen ray in 15 per cent. The authors concluded that in their hands roentgenography was not an effective means of making an early diagnosis of esophageal varices. We have not been able to find other series of cases in which a similar study was done.

Schatzki[4] reported the roentgen diagnosis of esophageal varices in 116 cases. He believed that the cause of the varices in these cases was either cirrhosis of the liver or thrombosis of the splenic vein, but did not give the number of each. While the total number of cases with cirrhosis examined was not given, he stated that esophageal

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TABLE I

INCIDENCE OF ESOPHAGEAL VARICES BY ESOPHAGOSCOPY IN CIRRHOSIS OF THE LIVER

	No. of Cases	Cases with Varices	Per Cent
History of hemorrhage	64	51	78.1
No history of hemorrhage	108	57	52.7
Total	172	108	62.7

varices were demonstrable roentgenographically in about 50 per cent of all cases. The diagnostic criteria to establish the underlying disease in the cases reported were not given. It would appear to the authors that, in view of the differences of opinion as to diagnostic accuracy of the roentgen diagnosis of esophageal varices, further information would be of value.

MATERIAL AND METHODS

One hundred and seventy-two patients with cirrhosis of the liver were studied. In every case the diagnosis was confirmed by histopathologic evidence: in 171 cases by punch needle biopsy and in 1 case by peritoneoscopic biopsy. Esophagoscopy, using the Eder-Hufford esophagoscope, was performed in each patient. This instrument is fitted with a telescope furnishing four-diameter magnification. In each case roentgen study was done, some before, some after esophagoscopy, with specific instructions to the radiologist to search for esophageal varices. The case material was gathered from three university-affiliated teaching hospitals with separate roentgen-ray departments under the direction of radiologists of wide experience.

RESULTS

Table 1 presents the incidence of varices in the series diagnosed esophagoscopically. In the whole series of 172 cases, 108 patients, or 62.7 per cent, had esophageal varices. When the cases are separated into those having a history of hemorrhage, 51 of 64 patients with such history, or 78.1 per cent, had varices, while 57 of 108 patients with no history of hemorrhage, or 52.7 per cent, had varices. That varices in cases of cirrhosis with hemorrhage would be present in many cases is quite well known, but an incidence of 52.7 per cent of varices in cirrhosis uncomplicated by hemorrhage is of great interest and is reported more fully elsewhere.[1]

Table II compares the esophagoscopic and roentgen diagnosis of esophageal varices. It will be noted that only 24 cases in the series were diagnosed by roentgen ray in contrast to 108 cases esophagoscopically found.

In this series only 22 per cent of the cases diagnosed by esophagoscopy were reported present by roentgen study. A negative roentgen report was given in 84 cases which had varices by esophagoscopy.

In Table III the cases are separated by the presence or absence of a history of hemorrhage and the comparative findings by esophagoscopy and roentgen study. It is to be noted that when there was a history of hemorrhage, varices were found in 29.6 per cent of the cases by roentgen ray and 78.1 per cent by esophagoscopy. Thus, varices were diagnosed roentgenologically in over a third, 37.2 per cent, of those found at esophagoscopy. In the cases with no history of hemorrhage, varices were diagnosed by esophagoscopy in 57 cases, or 52.7 per cent, while only 5 cases, or 4.6 per cent, were noted by roentgen examination. Less than 10 per cent of this group without hemorrhage was diagnosed roentgenologically as compared with esophagoscopy.

TABLE II

COMPARISON OF ESOPHAGOSCOPIC AND ROENTGEN STUDY IN DIAGNOSIS OF ESOPHAGEAL VARICES IN 172 CASES OF CIRRHOSIS

No. of cases with varices by esophagoscopy	108
No. of cases with varices by roentgen ray	24
Varices by esophagoscopy, negative roentgen findings	84

TABLE III

COMPARATIVE ESOPHAGOSCOPIC AND ROENTGEN DIAGNOSIS OF ESOPHAGEAL VARICES IN CIRRHOSIS WITH AND WITHOUT A HISTORY OF HEMORRHAGE

	History of Hemorrhage	Per Cent	No History of Hemorrhage	Per Cent
Total cases	64	100	108	100
Varices diagnosed by esophagoscopy	51	78.1	57	52.7
Varices diagnosed by roentgen ray	19	29.6	5	4.6

DISCUSSION

Esophagoscopy, using the semi-flexible Eder-Hufford esophagoscope, has been without any danger to the patient and can be done as an outpatient procedure in the same manner as gastroscopy. It appears to be the most accurate means of diagnosing esophageal varices available clinically. In this study, reliance on roentgen diagnosis of esophageal varices would have given an erroneously low incidence of esophageal varices in cirrhosis. It is interesting to note that roentgen diagnosis was four times more accurate when a history of hemorrhage was present than in the absence of such history. We attribute this to the fact that larger varices are more apt to be present in bleeding cases than in cases of cirrhosis without hemorrhage. We have also observed that when there is a positive roentgen diagnosis, the varices by esophagoscopy will usually be large and extensive. It would appear from this study that dependence on roentgen diagnosis will only uncover 22 per cent of the cases that can be found by esophagoscopy. Certainly, intensive effort to improve the present roentgenologic methods of diagnosis of esophageal varices appears to be needed.

SUMMARY

A study of 172 cases of proved cirrhosis of the liver is presented. Relative diagnostic merit of esophagoscopic and roentgen diagnosis of esophageal varices is compared. In this series, varices were present in 62.7 per cent of the cases by esophagoscopy and in 14 per cent by roentgen ray.

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THE ROENTGENOGRAPHIC DIAGNOSIS OF THE ARNOLD-CHIARI MALFORMATION*

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THE Arnold-Chiari malformation is a downward transposition of the cerebellum and medulla to the cervical portion of the spinal canal. The cerebellar component of this anatomical disarrangement was described initially by Arnold[2] in 1894 in a detailed account of a newborn monster with a large lumbosacral meningocele. The cerebellum in this instance extended inferiorly into the mid-cervical region as a tongue-like prolongation. Chiari,[3,9] in 1895, independently reported the medullary feature of the deformity characterized by bulging of the lower portion of the medulla against the cervical spinal cord. Relatively recently, Russell[12] called attention to the association of meningomyelocele with the Arnold-Chiari malformation. Her observations were amplified in a classic monograph dealing with the pathology of hydrocephalus.[11] In the latter communication, Russell[12] emphasized the constancy with which the Arnold-Chiari deformity accompanies advanced forms of spina bifida with hydrocephalus. So uniform was this pathological association that there was not a single example in her autopsy material of meningomyelocele without a coexistent Arnold-Chiari malformation.

There is a tendency in the literature to fail to distinguish the Arnold from the Chiari component of the anatomic malformation. Although the two components usually co-exist, either one may occur alone or take predominance. The descriptions in the radiologic literature are concerned only with the complete, uncomplicated Arnold-Chiari syndrome and consequently require critical analysis and revision.[4,6] It is the purpose of this paper to describe the underlying pathology of this entity, examine the present roentgen criteria for diagnosis and discuss the anatomic basis for the myelographic findings.

Clinically, the Arnold-Chiari malformation may produce (1) signs of a cerebellar disturbance (incoordination, nystagmus, intention tremor, etc.), (2) manifestations of brain stem and cord compression (pyramidal tract signs, sensory disturbances and variable degrees of lower cranial nerve involvement) and (3) obstructive hydrocephalus. The clinical state, therefore, by reason of its profusion of neurological findings, may simulate syringomyelia, syringobulbia, disseminated sclerosis, basilar arachnoiditis or tumor of the cerebellum, brain stem or cervical cord.[5,8,10] This medullocerebellar malformation has been associated with certain skeletal anomalies, such as platybasia, Klippel-Feil syndrome, anomalies of the craniovertebral border and rachischisis, but no apparent relationship to spina bifida occulta has been established.[7]

The pertinent pathological findings of the complete Arnold-Chiari deformity include (1) downward prolongation of the inferior portion of the cerebellar hemispheres for a variable distance within the cervical spinal canal, and (2) caudal displacement of the medulla and spinal cord. The medulla is displaced inferiorly and dorsally upon the upper cervical cord producing a prominent posterior bulge at the medullocervical junction. The caudal displacement of the medulla and cervical cord results in elongation and upward obliquity of the cervical roots as they ascend to exit at their respective intervertebral foramina. Frequently, dense adhesions are present between the cerebellar prolongations and medulla.

Recent experience with a case of Arnold-

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Chiari deformity and a number of other upper cervical obstructive lesions prompted review of the generally accepted myelographic criteria for establishing specific pathological diagnoses in this region.

CASE REPORTS

CASE 1. *Meningioma at C1–2.* This thirty-nine year old housewife was admitted to the hospital on February 9, 1951, because of unsteadiness of gait and progressive stiffness of all extremities for the preceding eight months. Early in her course, she developed numbness of both hands and weakness in grip. Her gait became grossly unsteady but there were no episodes of falling. Twelve days before, roentgenograms of the skull and cervical spine taken at another hospital were negative. Lumbar puncture performed there failed to disclose any abnormality of the spinal fluid. She was then discharged and during the eight days preceding the present hospitalization developed severe diffuse headache, vomiting and stiffness of the neck. There were no symptoms referable to the urinary or rectal sphincters.

On admission, the patient was apprehensive and in acute cervical discomfort. There was nystagmus to the right on right lateral gaze but the cranial nerves were otherwise physiologically intact. The fundi appeared normal. Slight nuchal rigidity was present. There was moderate spasticity of both upper and lower extremities with symmetrically exaggerated deep reflexes, bilateral ankle clonus and Babinski signs. Sensory perception was intact throughout without a detectable sensory level. Lumbar puncture revealed clear colorless fluid under normal pressure. The spinal fluid protein was 30 milligrams per cent and there were no cells. Pantopaque myelography, performed on February 13, 1951, disclosed a complete block at the level of C1-2 with bilateral concavity defects (Fig. 1). Several hours after myelography the patient developed marked respiratory difficulty and urinary retention. Further motor loss supervened and sensory changes appeared. Therefore, immediate upper cervical and suboccipital decompression was performed. Intradural exploration was limited owing to the patient's extremely poor condition, but there was some posterior kinking of the cord at C1 with filmy arachnoidal adhesions about its posterior aspect. Following division of these adhesions, the cord appeared to resume its normal position and the dura was left partially open. The postoperative course was characterized by partial recovery of motor power of the upper and lower extremities and regression of the sensory changes. However, manometric determinations performed on the twentieth postoperative day demonstrated complete block in spinal fluid dynamics and the spinal fluid protein was 200 milligrams per cent. With the patient's general status improved, re-exploration of the upper cervical region was carried out on March 7, 1951. The spinal cord was buckled posteriorly at C1–2 and displaced somewhat toward the left. After rotating the spinal cord, a firm nonsuckable lobulated pinkish-white mass was visualized which occupied the anterior intradural space extending principally to the right. The encapsulated tumor measuring 3.0 by 1.5 by 1.0 cm. in size was removed piecemeal without difficulty and proved to be a meningioma.

FIG. 1. Case 1. Meningioma C1–2. Note bilobate defect.

The patient's course, thereafter, was one of slow progressive return in motor function. She received an intensive course of physiotherapy

FIG. 2. Case II. Arnold-Chiari malformation. Central incisura absent.

and at the time of hospital discharge on May 23, 1951, was ambulatory with almost full recovery of strength and dexterity in her hands. She was last seen in April, 1953, and during the preceding six months had attended all her household duties which included the care of three children. The deep reflexes were hyperactive throughout and Babinski signs were present bilaterally. Fine skilled movements of both hands were intact, coordination good and the power in the extremities moderate.

CASE II. *Arnold-Chiari Malformation.* This thirty-six year old single white female was admitted to the hospital on September 18, 1951, with complaints of progressive weakness and spasticity of all extremities of five years' duration. She had been able to walk with some difficulty until three years preceding admission, but developed accelerated loss of power in both lower extremities thereafter so that she was bedridden for the past two years. During the latter period she had frequent suboccipital headaches, progressive diminution in strength of voice and was aware of spontaneous flexor spasms of both lower extremities. Six months before admission, she developed progressive disability of both hands so that she was unable to grasp objects or feed herself. There was difficulty in swallowing, frequent nasal regurgitation and almost complete loss of voice except for low whisper. There were no visual disturbances or episodes of vomiting. Occasional bouts of urinary incontinence occurred.

On admission, the patient appeared pale and chronically ill. Horizontal and vertical nystagmus accompanied gaze in all directions. The gag reflex was absent. Swallowing of liquids was followed by nasal regurgitation. The voice was but a whisper. Power in the sternomastoid and trapezius muscle groups was grossly re-

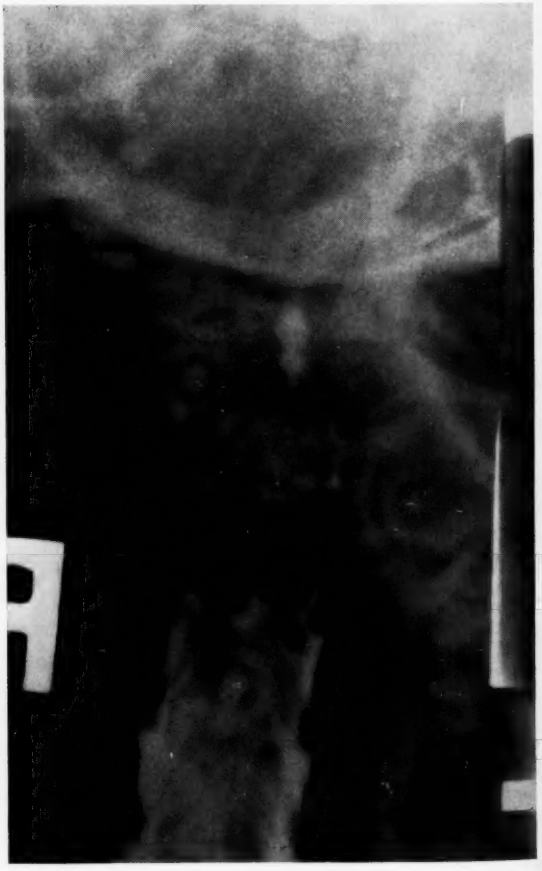

FIG. 3. Case III. Meningioma C2–4. Note bilobate defect and central incisura.

duced. The optic fundi appeared normal and the remainder of the cranial nerves were physiologically intact. There was no limitation of motion of the cervical spine or tenderness on palpation of the cervical spinous processes. There was an advanced quadriplegia present with feeble voluntary flexor movements of the fingers of the left hand and slight dorsal and plantar flexor movement present at both ankles. The deep reflexes were symmetrically exaggerated. Ankle clonus, patellar clonus and Babinski signs were present bilaterally. Pin-prick and light touch perception were impaired over the entire body including upper and lower extremities to the level of the clavicles. Position sense and deep pain sensibility were impaired in both lower extremities but vibratory perception was intact.

Roentgen examination of the skull, cervical spine and chest were normal. Lumbar puncture disclosed clear colorless fluid under an initial pressure of 150 millimeters of water. Manometric determinations indicated a partial spinal fluid block. The spinal fluid protein was 75 milligrams per cent and the Pandy reaction was elevated. Pantopaque myelography revealed a partial block in the upper cervical region at the level of C1–2 with concavity defects (Fig. 2). Some of the pantopaque, however, passed upward into the basilar cisterns. The myelographic study was interrupted by the patient's sudden lapse into coma with loss of spontaneous respirations. Supportive measures were instituted and, after an elapse of some eight hours, operative intervention was carried out.

Complete laminectomy of C1 through C3 and suboccipital craniectomy were performed. The dura was grossly thickened and densely adherent posteriorly to the pia arachnoid. At the inferior border of C1, applied to the dorsal aspect of the cord, was a moderately thick bluish-gray elongated mass which had a definite folial surface pattern. Further exploration proved this to be cerebellum densely adherent to the posterior aspect of the spinal cord. The cervical roots of C1, 2 and 3 were identified on each side and these pursued a slightly oblique upward direction to exit through the dura. There were numerous bridging vessels from the cerebellar prolongation to the cord and, except for a biopsy of the cerebellar tissue, the anatomical situation was left undisturbed. A moderately dense circular arachnoidal wing was found at the level of C2–3 below which droplets of pantopaque appeared to have been arrested in their cephalic flow. Decompression of the region included uncapping of the posterior rim of the foramen magnum. The patient recovered spontaneous respirations by the conclusion of the operative procedure and regained consciousness by the second postoperative day. At that time a sensory level was evident at the lower border of the mandible. By the sixth postoperative day, the patient was able to swallow fluids without regurgitation. Three days later, voluntary movements of the distal portions of all four extremities returned. Over the next several weeks, she manifested slow progressive recovery of voluntary flexion and extension of the thighs and legs as well as some recovery in the use of her hands for grasping of objects. At the time of discharge, December 8, 1951, she had residual evidence of bilateral pyramidal tract signs with hyperflexia, ankle clonus and bilateral Babinski signs. She was able to carry on ordinary conversational speech without manifesting weakness of her voice and she had no symptoms referable to the urinary or rectal sphincters. She had not recovered motor function to the degree that she could walk without assistance.

Case III. *Meningioma (Anterior C2–4)*. This sixty-eight year old housewife was admitted to the hospital on February 2, 1952, complaining of recurrent upper cervical pain, progressive stiffness of all extremities, bilateral weakness of grip and unsteadiness in gait of seven months' duration. During the preceding several months she was aware of numbness of the finger tips of both hands, and occasional involuntary muscular jerks of both lower extremities.

On examination, no abnormal cranial nerve findings were noted nor was there any tenderness or limitation of motion of the cervical spine. There was increased resistance to passive stretch in all extremities with marked symmetrical hyperreflexia. Bilateral Babinski signs and ankle clonus were present. In addition, a terminal tremor was manifest on finger-to-nose and heel-to-knee testing. However, no discrete sensory level could be obtained for superficial pain or light touch perception. Appreciation for hot and cold stimuli was reduced in the right lower extremity. Vibratory, deep pain, position, skin-writing and kinesthetic sensibility were ntact throughout.

Preliminary films of the cervical spine were negative. Lumbar puncture revealed a block with clear, colorless fluid containing 100 milli-

grams per cent of protein. On February 6, 1952, cervical myelography confirmed the manometric findings, demonstrating an almost complete block at C_{3-4} with an intradural extramedullary filling defect (Fig. 3).

Exploratory laminectomy, C2 through C_4, was performed on February 9, 1952, under endotracheal anesthesia. The dura was moderately tense and without pulsation. Upon opening the dura, the dorsal aspect of the cord immediately presented, being buckled considerably posteriorly. Following division of the posterior root of C_4 on the left side, the cord was mobilized sufficiently to expose a pinkish-red, firm encapsulated lobulated mass which occupied the anterior intradural space. It was necessary to divide the anterior and posterior roots of C_5 on the right in order to accomplish complete removal of the tumor which extended from the level of C2 through C_4. The patient tolerated the procedure well and the postoperative course was uneventful. She was discharged from the hospital on February 22, 1952, her thirteenth postoperative day, and by then she had considerable increase in strength of both hands and marked improvement in stability of gait. The microscopic diagnosis was meningioma with psammoma bodies.

When seen six months postoperatively, she had no residual subjective symptoms and her neurological status was normal.

DISCUSSION

In the pure uncomplicated Arnold-type malformation, myelography demonstrates an obstructive cervical lesion with an inferior bifid lobulated border. The latter is produced by the inferior border of the herniated cerebellar hemispheres, the central incisura corresponding to the space between the cerebellar hemispheres. Cases I and II demonstrate that this picture is not pathognomonic of the Arnold malformation. As a matter of fact, it may be produced by any lobulated intradural extramedullary tumor. Similarly, in the presence of dense adhesions over the cerebellum, the central incisura may be obliterated and hence the myelographic pattern will resemble that commonly seen with intradural extramedullary lesions, *e.g.*, neurofibroma or meningioma.

The combined Arnold-Chiari deformity or the Chiari component per se results in buckling and downward displacement of the medulla against the cervical cord. Consequently, if only the inferior portion of the lesion is visualized, the typical bilobate pattern may not be seen. Instead, one may find a block with a deformity of the myelographic column which may or may not be symmetrical depending on the character of the medullocervical buckling. However, if sufficient pantopaque passes up to delineate the superior border of the lesion and the latter is poorly defined, the diagnosis of tumor is less likely. Similarly, distortion of the normal contour of the cisterna magna favors the diagnosis of the Arnold-Chiari malformation.

It can readily be seen that the roentgen findings described in the literature as being characteristic of the Arnold-Chiari syndrome may be simulated by benign intradural tumors. The Chiari syndrome may exist in the absence of the so-called typical myelographic appearance. In addition, the degree of cerebellar adhesions may influence the type of myelographic defect visualized. The problem of differential roentgen diagnosis of such defects occurring in childhood or adolescence rarely presents itself inasmuch as high spinal cord tumors in this age group are extremely uncommon. The co-existence of such a myelographic pattern with hydrocephalus heavily favors the diagnosis of the congenital malformation. In adults, however, the problem may be more difficult and the clinical neurological picture assumes considerable importance in weighing the myelographic diagnosis one way or another. In any event, one is dealing with a high spinal obstructive process, partial or complete, which requires surgical intervention. Consequently, the exact specific preoperative diagnosis, though desirable, may not always be made from the roentgenographic findings alone and may have to await surgical exploration.

SUMMARY

1. The pathology of the Arnold-Chiari malformation is reviewed.

2. The anatomical basis for the myelographic findings of this syndrome is discussed.

3. The roentgen criteria for the diagnosis of this entity are critically examined.

4. Two cases of high cervical meningiomas and one case of the Arnold-Chiari malformation are reported.

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HYPEROSTOSIS FRONTALIS INTERNA AMONG THE AGED*

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THE name of Morgagni's syndrome was proposed by Henschen[2] (1949) in an excellent monograph for the triple findings of hyperostosis frontalis interna, obesity and virilism. Although much has been written about hyperostosis frontalis interna since Morgagni's early description, the cause for this curious finding is still only vaguely understood. This report concerns studies to determine the incidence of hyperostosis frontalis interna and its association particularly with obesity and hirsutism in a group of otherwise normal aged subjects.

METHOD AND RESULTS

Roentgen studies were made of the skeleton of 128 residents in the Home for the Jewish Aged in Philadelphia. These comprised 79 females and 49 males ranging in age from fifty-eight to ninety-six years. The degree of hyperostosis was divided into minimal, moderate and advanced, following roughly the classification of Moore.[3] (Fig. 1).

Hyperostosis frontalis interna was found in 49, or 62 per cent, of the 79 women and in none of the men (Table I). In only 3 cases was the hyperostosis marked; it was moderate in 16 and minimal in 30 cases.

The association of virilism and obesity was analyzed and not found significant (Table II).

Fig. 1. Moderate hyperostosis frontalis interna in a healthy woman eighty years of age, not overweight, with hirsutism of the face.

DISCUSSION

The high incidence of hyperostosis frontalis interna found by us in elderly women has been established by many previous observers, all tabulated by Henschen. Typical among these are the findings of Eldridge and Holm[1] who encountered an incidence of hyperostosis frontalis interna in 72 per cent of 200 women over forty years of age. Henschen found that hyperostosis frontalis occurred 100 times more frequently in women than in men. While his data led him to believe that the triad of hyperostosis frontalis interna, virilism and obesity was a valid syndrome, our findings do not bear out this conclusion. Yet we favor the concept that hyperostosis frontalis interna, like obesity and hirsutism, are frequent tertiary sex characteristics of the climacterium in women.

SUMMARY

Among 128 residents of the Home for the Jewish Aged in Philadelphia, hyperostosis frontalis interna was observed in 62 per cent of the women and not once among the men. Obesity and virilism occurred frequently among the women, but not sig-

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TABLE I

THE INCIDENCE OF HYPEROSTOSIS FRONTALIS INTERNA IN A GROUP OF AGED WOMEN

Age Class in Years	Age Class Distribution of All Women Studied	Age Class Distribution of Hyperostosis Frontalis Interna Cases
50–59	1	1
60–69	7	5
70–79	48	31
80–89	21	11
90–99	2	1
Total	79	49

nificantly in association with hyperostosis frontalis interna. These findings suggest to us that hyperostosis frontalis interna, like obesity and hirsutism, is a tertiary sex characteristic in women.

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TABLE II

THE INCIDENCE OF HIRSUTISM, OBESITY AND HYPEROSTOSIS FRONTALIS INTERNA IN A GROUP OF AGED WOMEN

	Number of Cases	Hirsutism		Obesity	
		No.	Per cent	No.	Per cent
Hyperostosis frontalis interna cases	49	40	82	10	20.4
Cases without hyperostosis frontalis interna	30	23	76	4	13.3

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BENIGN ULCER OF THE GREATER CURVATURE OF THE STOMACH

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BENIGN peptic ulcers of the greater curvature of the stomach are stated to be rare in comparison to malignant ulcers in a similar location. A recent review of the literature[1] revealed only 31 reported cases. Verbal reports from numerous observers would indicate that the actual incidence of benign greater curvature ulcers is much higher than the reported cases.

The present case is striking because of the presence of those characteristics most often associated with carcinoma.

CASE REPORT

A sixty-one year old white boilermaker entered the hospital for repair of an inguinal hernia. This was his chief complaint. Routine history revealed some upper gastric distress for about two years. He had occasional nausea and vomiting without evidence of hematemesis or melena. He had lost 15 pounds in the past six months. No food-pain relationship could be elicited. The patient had some urinary complaints with nocturia two to three times and increasing difficulty in the mechanism of urination. The past history did not reveal any sig-

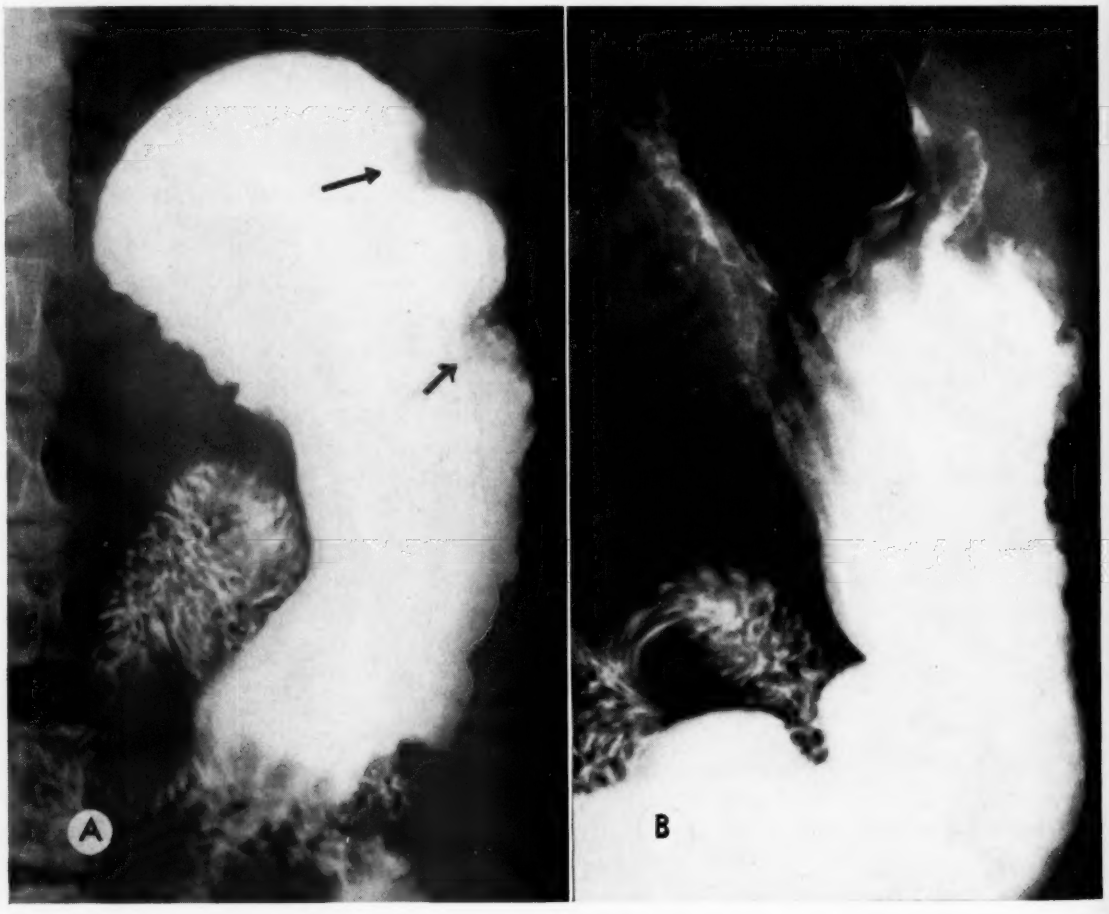

FIG. 1. (*A*) Large ulcer along the greater curvature of the fundus of the stomach. The mouth measured 3 cm., base 2 cm., depth 2 cm. Adjacent portions of the stomach are indented; arrows indicate prominent edges. (*B*) Twelve days later. The size of the ulcer has decreased considerably.

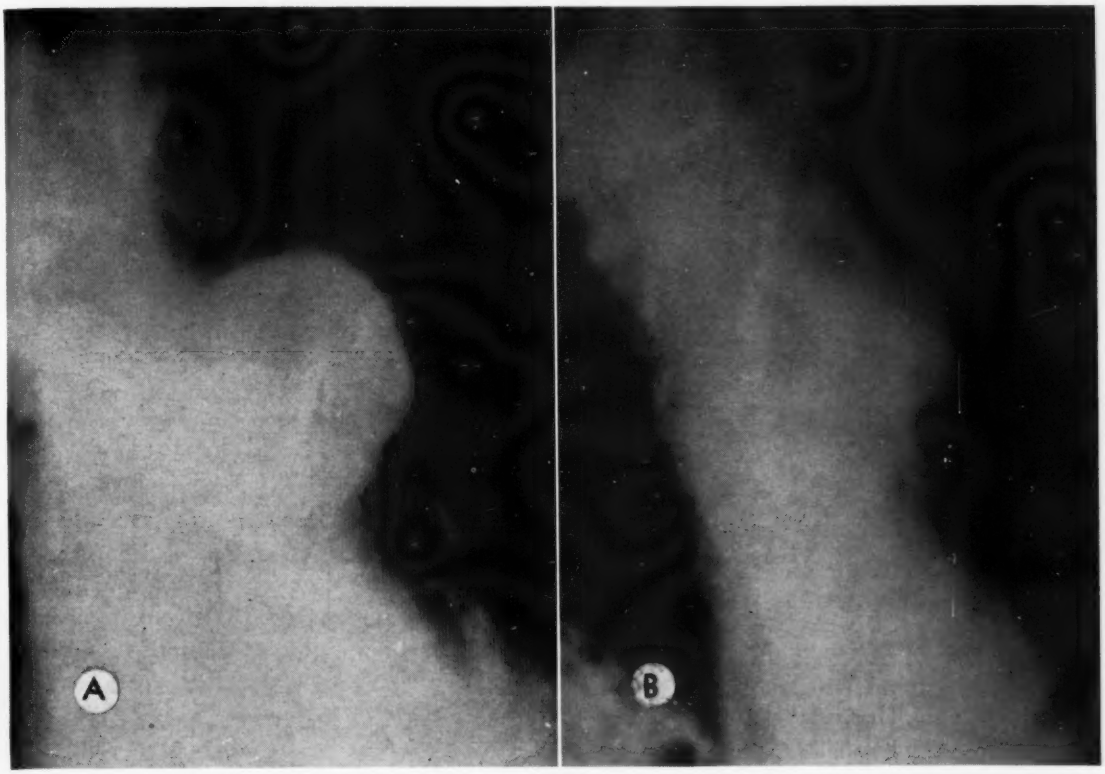

Fig. 2. (*A*) (*B*) Comparable views to show decrease in size in twelve days. Note wide mouth of the ulcer in relation to base and depth. Also note the decrease in size has been chiefly from filling in of the base.

nificant facts. An appendectomy had been performed six years previously.

Physical examination revealed a well developed and well nourished white male. Blood pressure was 100/60. Examination of the head and neck as well as the heart and lungs revealed no abnormalities. The abdomen was soft without masses. A large left indirect inguinal hernia was present. The prostate gland was slightly enlarged. Laboratory studies revealed a red blood cell count of 4.3 million, white blood cell count of 6,900, and a hemoglobin of 11.7 gm. The differential count was normal. Urine and serology were normal. The nonprotein nitrogen was 26 mg. per cent. A gastric analysis showed no free HCl in the fasting specimen with a total of 24 degrees. The test for blood was slightly positive. The second specimen taken after an alcohol test meal showed 11.2 degrees free HCl and a total of 20 degrees. Cystoscopic examination revealed a constriction at the bladder neck. A cholecystogram was normal. The gastrointestinal series revealed a large crater shadow along the greater curvature side of the fundus of the stomach. This actually lay within the normal projected outline of the stomach contour. It measured 3 cm. across at the base and 2 cm. at the apex. Areas of decreased density were present at the margins and base appearing as irregular filling defects. The remainder of the stomach appeared normal.

Course in the Hospital. The patient was treated medically for a gastric ulcer for twelve days with improvement in his gastric symptoms. A repeat gastrointestinal examination at this time revealed a definite measurable decrease in the size of the barium-filled crater. The base of the ulcer was still wider than the outpouched portion; the margins were smooth. One week later a total gastrectomy with esophagojejunostomy was performed. The spleen was removed and lymph nodes from the lower esophagus, the anterior pancreas region, and the pyloric region of the stomach were included in the pathological specimen.

Pathological Findings. The specimen consisted of the entire portion of a surgically resected stomach. Along the greater curvature in the upper third of the specimen there was a large

excavated crater with raised edges. The crater measured 2 by 2 cm. with a depth of 1 cm. The floor of the crater was covered with a greenish-gray mantle having the gross appearance of granulation tissue. The rugae pointed toward the crater ending in the raised edges of the mass. The walls of the ulcer were white, indurated and gave a grating sensation when cut. On section, the ulcer extended through the wall of the stomach to the serosa. At the point where the serosa was involved, a puckering was present with a mass of fat and fibrous tissue. The spleen was also present.

A 2 by 2 by 0.5 cm. lymph node from the pyloric region was included as well as a lymph node from the esophageal region measuring 8 by 5 by 5 mm. These lymph nodes were indurated and on section were glistening yellow in color. Two more lymph nodes about 1 cm. in size from the area anterior to the pancreas were studied and these were similar in appearance.

Microscopic Study. Sections from the ulcer margins showed normal gastric mucosa with an intact muscularis. In the ulcer edges a tremendous fibrous tissue reaction was present with lymphocytes, both singly and in follicle form infiltrating the fibrous tissue and also the muscularis mucosae. The floor of the ulcer was covered by granulation tissue and masses of necrotic fibrous type cells. The spleen was normal in appearance. Sections from the lymph nodes showed essentially normal architecture with hyperplastic changes and normal maturation of the lymphocytes. The capsules were thickened. Additional sections were taken from the ulcer walls and these showed a similar pattern with lymphocytes and occasional eosinophils in the submucosa. No tumor cells were identified in any of the sections.

Pathological Diagnosis: (1) Gastric ulcer, greater curvature, with marked chronic gastritis; (2) hyperplastic lymph nodes beside esophagus, anterior to pancreas and at the pylorus; (3) spleen.

The postoperative course was uneventful. Three months later the inguinal hernia was repaired. The patient was last seen six months later well and without clinical or laboratory evidence of disease.

Comment. The roentgenologic features of this ulcer favored the diagnosis of a malignant lesion. These included (1) position on the greater curvature of the fundus, (2) location within the expected projected outline of the stomach, (3) large size, and (4) a width greater than the depth. In addition, the history of vague gastric discomfort with a weight loss of 15 pounds, no free hydrochloric acid and low total acidity were factors contributing to the clinical diagnosis of possible malignancy. The decrease in size following ten days of therapy was difficult to evaluate.

SUMMARY

A case of a large ulcer situated along the greater curvature of the fundus of the stomach is presented. This had all the accepted characteristics of a malignant ulcer but microscopic examination revealed a benign peptic ulcer.

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INVERTED DUODENUM

CASE REPORT*

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INVERTED duodenum is a congenital anomaly which involves the second and third portions of the duodenum. There have been approximately 56 cases reported in the literature to date. The incidence of this anomaly according to Feldman and Morrison[1] in approximately 20,000 gastrointestinal roentgen examinations is 0.07 per cent. There is a much higher incidence of this anomaly in males,[2] about 70 per cent to 30 per cent in females.

This anomaly is thought to be caused by a persistence of the dorsal mesentery and an error of rotation of the midgut. This causes a mobile duodenum with either shortening or lengthening of the caudal segments of the duodenum. Since the duodenum is considered mobile, there have been four types of duodenum inversum observed. These four types are well outlined in the article by Feldman and Morrison. The purpose of this paper is to present one additional case of the second type of this rare anomaly.

CASE REPORT

A twenty-three year old soldier entered our hospital with a history of upper abdominal pain and nausea prior to meals for the past eight months. During this time he had occasional vomiting of food and coffee-ground material. Food and milk relieved the pain most of the time. He had lost 20 pounds in weight during this time. A diagnosis of possible duodenal ulcer was made four months after the symptoms began. He was placed on antispasmodics and antacids with only temporary improvement. This treatment was continued for four months, and inasmuch as his symptoms persisted he was sent to our hospital for an upper gastrointestinal series.

Physical examination on admission to our hospital revealed a well developed and well nourished male in no acute distress. There was moderate tenderness in the upper epigastrium on deep palpation. The remainder of the physical examination was not remarkable.

The report of the gastrointestinal roentgen examination was as follows: Barium flows freely into the stomach. The esophagus, stomach and first portion of the duodenum are normal in size and position. The rugal pattern is normal. Peristalsis is somewhat hypoactive. There is no evidence of ulceration or deformity of the stomach or duodenal bulb. The duodenal sweep is inverted. The second and third portions of the duodenum pass over to the right side of the abdomen instead of to the left. This is a congenital anomaly which may result in some stasis in the duodenum, causing a duodenitis. There is no evidence of an ulcer crater in this loop. The remaining portion of the small intestinal pattern is normal. The diagnosis is duodenum inversum.

The patient was placed on an ulcer regimen following this examination. The anatomical anomaly that he has was explained to him in detail. He was informed that his symptoms were due to his duodenum being inverted. There was a marked improvement, with relief of pain and vomiting, in the following two weeks. He was returned to his original outfit on a full duty status. He was seen six months after his return to duty. During this time he had been able to carry on all his duties in a satisfactory manner in spite of interruptions in his ulcer regimen from time to time.

DISCUSSION

There may be no clinical symptoms associated with this anomaly but many cases have gastrointestinal symptoms suggestive of peptic ulcer. Symptoms are due to the delay in passage of the duodenal contents, according to Sandera.[3,4] It was possible for Feldman and Morrison to demonstrate roentgenologic signs of peptic ulceration in 5 of their cases. Occasionally

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Fig. 1. Duodenum inversum.

a peptic ulcer may be present with perforation requiring surgical intervention, as reported by Sheehan and Kelly.[5] Cholecystitis and pancreatitis are two other disease entities that may be produced from a change of position of the bile duct or stasis of the duodenal contents resulting in a backflow through the ducts into the pancreas and gallbladder.

The diagnosis of duodenum inversum is usually made during roentgenoscopy. The stomach empties normally in most instances. The entire curve of the duodenum must be examined carefully. Supine, prone, lateral and oblique views should be taken in all cases suspected of this anomaly. The case described above showed that the second and third portions of the duodenum were reversed and passed over to the right side of the abdomen (Fig. 1). Peristalsis was hypoactive. There was no evidence of an ulcer crater demonstrable.

The treatment of this condition consists of early diagnosis and conservative medical management. An explanation of this anatomical anomaly to the patient usually suffices in clearing up many of the psychosomatic aspects. When there is an associated lesion, treatment should be directed toward this disease. A bland diet with high caloric and high vitamin intake is desirable. In the case reported here the measures described above were completely satisfactory in controlling the patient's symptoms. Surgical intervention may become necessary when adequate medical therapy fails to relieve symptoms or to adequately treat one of the complications.

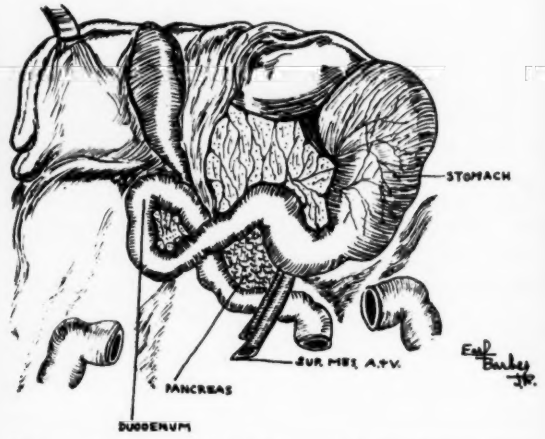

Fig. 2. Artist's sketch of inverted duodenum from a roentgenogram.

SUMMARY

A case of duodenum inversum is reported, bringing the total number in the literature to fifty-seven. A discussion of the symptoms, diagnosis and treatment found in all cases reported to date is presented.

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GAS IN THE SYMPHYSIS PUBIS DURING AND FOLLOWING PREGNANCY*

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RELAXATION of the pelvic joints with separation at the symphysis pubis is a normal occurrence during pregnancy. The evidence indicates that the separation occurs as the result of hormonal influence.[1,2,8,9,10,15] The presence of a streak of gas in certain joints under traction is also a well known phenomenon, but its common occurrence in the symphysis pubis during pregnancy does not appear to have been emphasized. A study of this gas shadow as seen on more than 3,000 pelvimetry films forms the basis of this report. In addition, roentgen changes in the symphysis pubis during and after pregnancy will be discussed and illustrated.

HISTORICAL

Fick,[5] in 1910, first observed gas in joint spaces while studying the effect of traction on the finger joints of cadavers. He saw the joints "light up" under the roentgenoscope and suggested that the traction produced "water steam." Dittmar,[4] in 1932, first reported a "cleft" in the knee joint during traction but he did not explain it. Following the publication of his paper, streaks of decreased density were described in the shoulder, wrist, and spine, but it was Magnusson,[12] in 1937, who first explained that decreased pressure existed when the "cleft" was visible, and that the decreased pressure apparently caused the liberation of gas from the joint fluid. It is now known that most of the potential joint spaces in the body can be demonstrated if enough traction is applied to produce low pressure within the capsule. It is generally assumed that traction on a joint lowers the pressure and thereby releases gas from the adjacent soft tissues or from the joint fluid. Thomas and Williams,[14] in 1945, stated that gas was visible in the knee joints of every person they examined at an altitude of 20,000 feet, even though there were no symptoms of "bends." An analysis of this gas has revealed nitrogen, oxygen, and carbon dioxide in concentrations approximately equal to those found in the blood.

The occurrence of gas in the symphysis during pregnancy has received very little attention. Dale,[3] in 1930, first described a "fissure" in the symphysis seen on roentgen studies, and Magnusson briefly mentioned that a gas streak had been seen in the symphysis pubis during pregnancy. No further reference to this gas streak has been found.

MATERIAL

One hundred and sixteen pelvimetric studies on primigravidae and 116 studies on multigravidae were analyzed with regard to age, race, width of symphysis pubis, and the presence or absence of a gas streak in the symphysis. The films which were analyzed were taken on consecutive primigravidae or multigravidae who were referred for pelvimetric studies for obstetrical reasons. The films were taken during late pregnancy or early labor, and in most instances views were secured with the patient in both the erect and the supine position. Two thousand eight hundred additional pelvimetric studies were reviewed in a search for unusual gas streaks, marked separation of the symphysis, and osseous changes in the medial portions of the pubic bones.

The width of the symphysis pubis was measured at the narrowest point in its middle one-third. The measurements were taken directly from the films and no correction factor was used for magnification.

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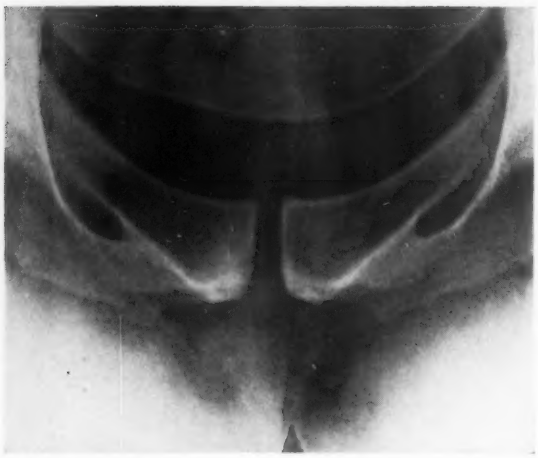


Fig. 1. Single gas streak in symphysis pubis.

ANATOMY

According to Gray's *Anatomy*[7] the pubic symphysis is an amphiarthrodial joint. The opposed surfaces of the pubic bones are covered by a thin layer of hyaline cartilage. These cartilaginous surfaces are connected by an intermediate lamina of fibrocartilage which varies in thickness in different subjects. It often contains a midline slit-like cavity (fissure) in its interior, probably formed by the softening and absorption of the fibrocartilage, since it rarely appears before the tenth year of life. It is not lined by synovial membrane. In parous women, Loeschcke[11] found at necropsy that the primary fissures are often exaggerated and secondary fissures frequently occur.

OBSERVATIONS

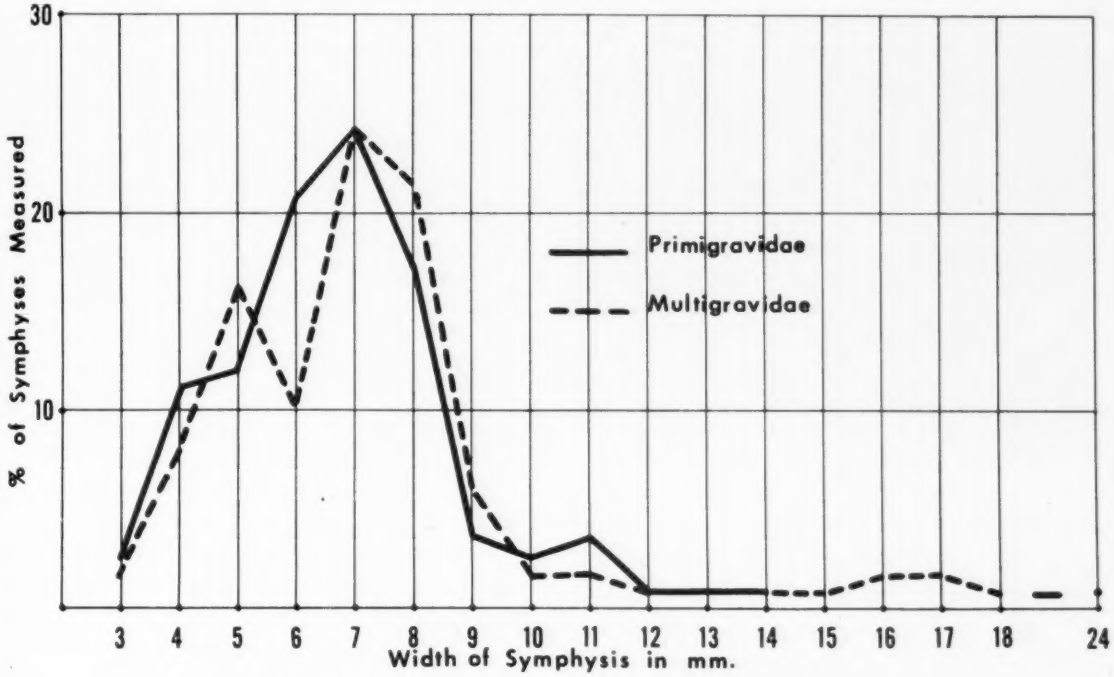
Gas in the symphysis pubis of pregnant women most commonly appears as a thin streak of decreased density running vertically in the center of the fibrocartilage. There are numerous variations in the gas pattern, but the most common appearance is shown in Figure 1. The gas streaks are usually thin, but on occasion may be as wide as 3 mm. (Fig. 2). Oblique or asymmetrical streaks may occur and multiple streaks are fairly frequent (Fig. 3). In any one individual the appearance of the gas streak or streaks tends to be the same during successive pregnancies. This suggests that the gas appears in the primary and secondary fissures described by Loeschcke.

Table 1 summarizes the incidence of gas streaks in the symphysis pubis of pregnant women at or near term. In the 232 roentgen studies, one or more gas streaks could be seen in 41.5 per cent of the patients, and the incidence was essentially the same in primigravidae and multigravidae. A gas streak was present in 54 per cent of colored women but in only 34 per cent of white patients. The reason for this significant racial difference is not apparent. Maternal age does not appear to play any part in the presence or absence of gas.

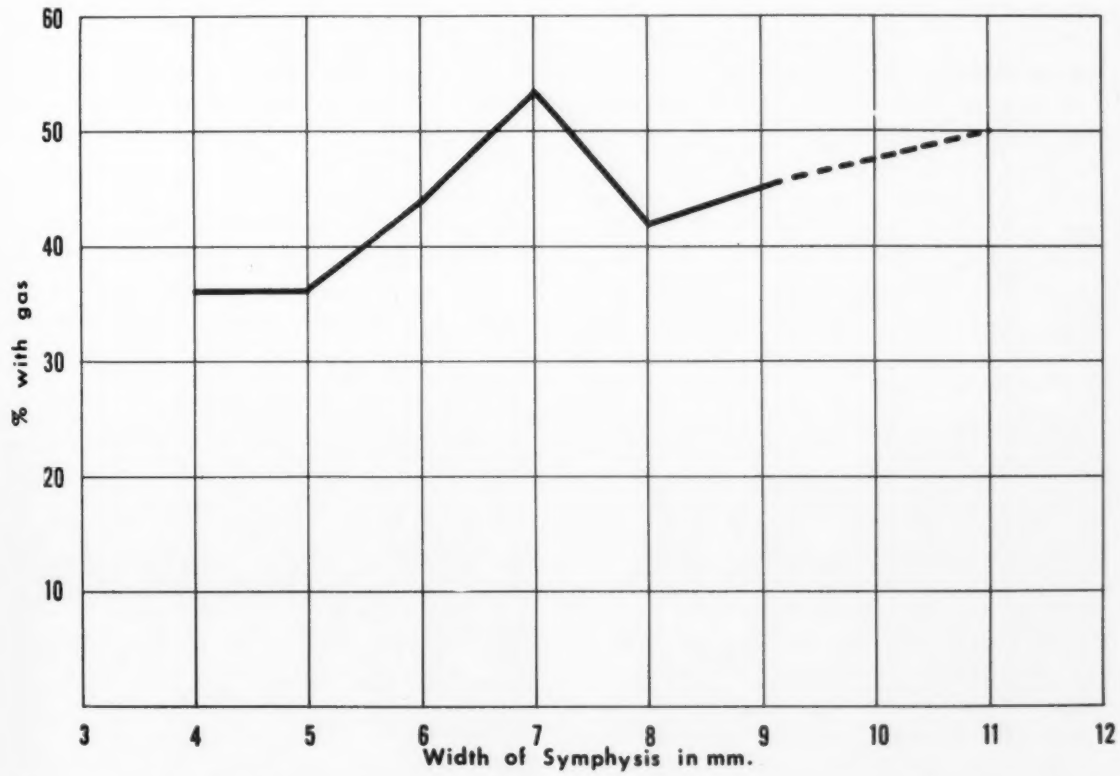
Graph 1 shows the relative frequency of the measured width of the symphysis in primigravidae and multigravidae at or near term. Most of the symphyses measured between 5 and 9 mm. The average width was 7.1 mm., as opposed to an average width of 4.1 mm. in nonpregnant women. In a small percentage of patients the width of the symphysis pubis measured 10 mm. or more. The widest symphyses seen in the 2,800 patients reviewed (but not included in Graph 1) measured 38 mm. in a multigravida and 44 mm. in a primigravida (Fig. 4).

Graph 11 shows the relationship between the presence of gas and the width of the symphysis. Gas was visible only if the symphysis measured between 4 and 11 mm. In the 232 patients there were 3 primigravidae and 10 multigravidae whose

Fig. 2. Unusually wide gas streak.



Graph I. The relative frequency of the measured width of the symphysis pubis.



Graph II. Relationship between the presence of gas and the width of the symphysis. Gas was not seen if the symphysis measured less than 4 mm. or more than 11 mm. The broken line indicates a small number of patients.

Fig. 3. Triple gas streak.

symphyses were wider than 11 mm. None of these 13 patients showed evidence of a gas streak. In numerous individuals not included in the tabulated series, a gas streak was seen during early pregnancy when there was only slight separation, but it always disappeared if the symphysis widened to 12 mm. or more, and in a few instances it disappeared when the symphysis widened to 10 or 11 mm.

Films were taken at intervals of one to two months in a few patients. In one individual a gas streak was visible at the tenth week of pregnancy, and in numerous patients it was visible before a fetal skeleton could be delineated. Although gas sometimes appeared quite early in pregnancy, there were numerous patients with little or no widening of the symphysis during the first trimester, and in these gas appeared only after additional widening had occurred in later pregnancy. In general, if gas was present during the first or second trimesters it persisted until term unless the symphysis widened to 12 mm. or more, in which case it disappeared.

When gas was present it could usually be seen on films taken in the erect, prone, and supine positions if there was only slight widening of the symphysis. If there was a moderate degree of separation, the symphysis was often 1 to 3 mm. narrower in the erect position, and the gas streak sometimes disappeared. Presumably, with this decrease in width there was no longer a relative vacuum to hold gas in the fibrocartilage. In one individual four films were secured as rapidly as possible, alternating the erect and supine positions. Gas was present on both supine films but not on either erect film, indicating that the gas appears and disappears within a few seconds and that the supine position favors distraction of the symphysis.

Table I

Percentage of Patients with Gas in the Symphysis Pubis

	No. Patients	Average Width of Symphysis in mm.	Per Cent with Gas
Primigravidae	116	6.7	41
Multigravidae	116	7.5	42
White	144	7.2	34
Colored	88	7.1	54

In selected cases films were taken with the patient standing on first one foot and then the other. It was not uncommon to see evidence of marked mobility of the pubic bones with a vertical shift of up to 1 cm. (Fig. 5). In the individuals with marked mobility there was never a gas streak in the symphysis.

It is well known that many pregnant women have pain and tenderness in the pubic region. The symptoms are more likely to occur with wider degrees of separation, although some with marked separation or mobility have no complaints.

Fig. 4. Marked separation (44 mm.) in a primigravida, prior to the onset of labor.

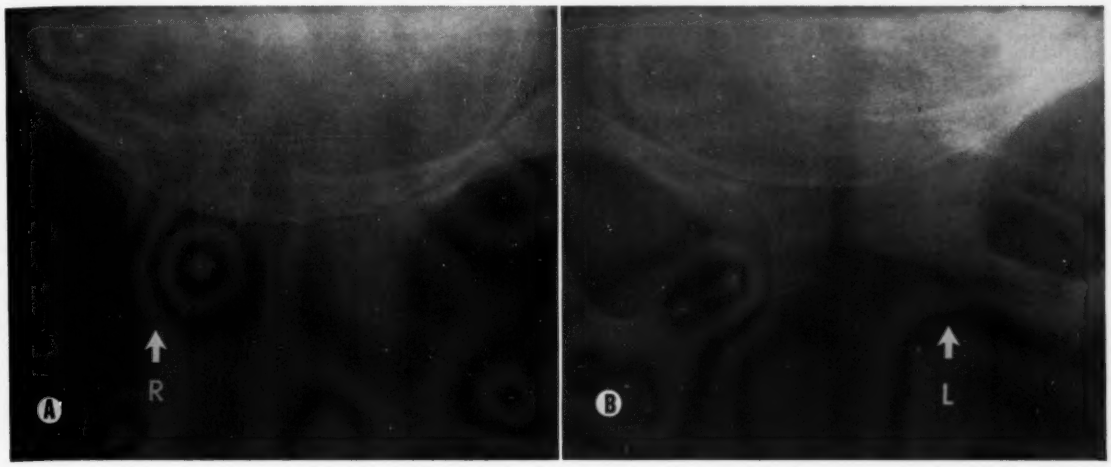


Fig. 5. Marked mobility at the symphysis pubis. The patient had no pain or tenderness. There is no gas in the symphysis. (*A*) Standing on the right foot. (*B*) Standing on the left foot.

For example, the patient whose films are shown in Figure 5 did not have pain or tenderness in the pubic area, while the patient whose film is seen in Figure 6 had such severe pain in the symphysis prior to delivery that she was unable to walk. There was no correlation between pain in the symphysis and the presence or absence of gas.

In postpartum patients the pubic symphysis gradually returned to normal width in a period varying between a few days and a few months. In most instances the gas disappeared within the first week following delivery, but in 2 patients it was seen as late as twenty days postpartum.

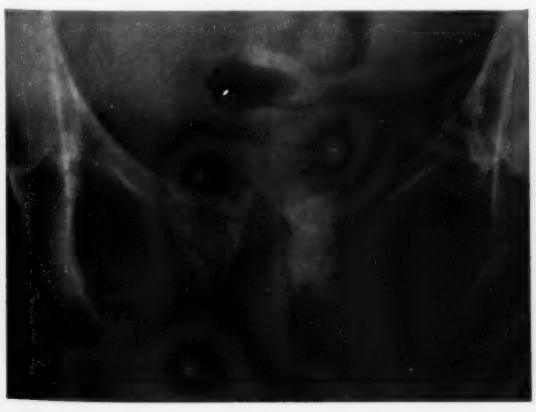


Fig. 6. Postpartum film in a multipara whose symphysis was still separated. There is marked sclerosis and minimal bone resorption secondary to earlier pregnancies.

OSSEOUS STRUCTURAL CHANGES

In addition to widening of the symphysis during pregnancy, there is often slight demineralization of the bones adjacent to the fibrocartilaginous disc, but the changes are not severe. In the postpartum period, however, marked changes may occur in the medial portions of the pubic bones. These consist of cyst-like areas of bone resorption, and there may be marked irregularity and sclerosis of the bones adjacent to the symphysis (Fig. 6, 7, and 8). The cartilage of the symphysis may be partially destroyed so that the bones lie closer together than average. The roentgen appearance may simulate other bone diseases. One patient who had pain in the

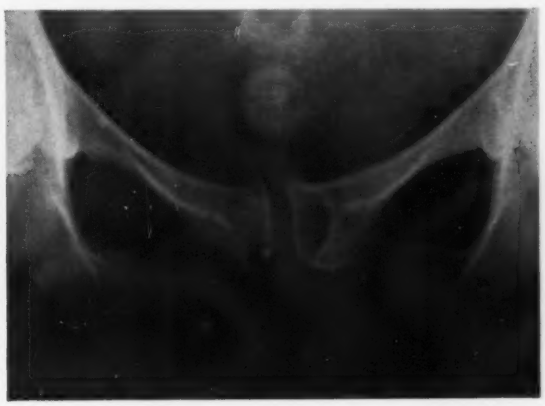


Fig. 7. Bone resorption following marked separation during a previous pregnancy.

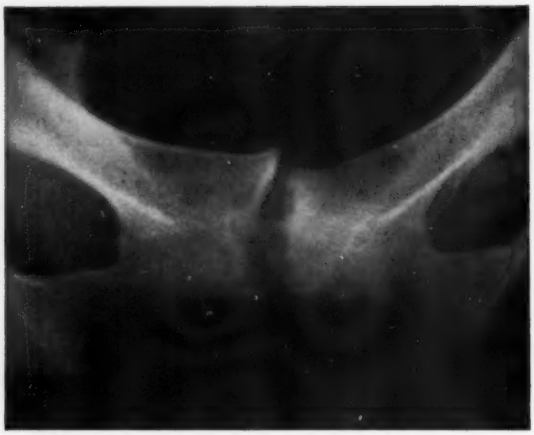


Fig. 8. Irregular bone resorption in a nonpregnant multipara. During her last pregnancy, three months before this examination, there was marked tenderness and severe pain in the region of the symphysis.

symphysis and bone destruction was first suspected of having tuberculosis or other infection of the pubis, and the correct diagnosis was made only when it was learned that she was three months pregnant. Her pain was due to the current pregnancy while the bone destruction was secondary to marked separation during a previous pregnancy.

The residual changes in the pubic bones tend to vary with the amount of separation during the previous pregnancies but the correlation is not absolute, and there are instances of sclerosis and irregularity following moderate separation, as well as pubic bones which appear normal following marked separation. The patient whose film is shown in Figure 7 had 26 mm. separation at the symphysis pubis during her previous pregnancy, and the medial margins of the pubic bones at that time were smooth and showed no evidence of the cyst-like changes which developed later.

DISCUSSION

Gas is frequently seen in joints of the extremities when traction is applied and it disappears as soon as the traction is released. It is believed that gas in the pubic symphysis occurs as a result of decreased pressure, just as it does in the shoulder, knee, and other joints.

Relaxation of the ligaments about the symphysis pubis during pregnancy allows lateral displacement of the pubic bones with widening of the symphysis, but the forces pulling or pushing the pubic bones laterally are not readily identifiable. In the supine position the weight of the innominate bones and the thighs could cause some separation at the symphysis, while in the prone position it is possible that direct pressure tends to push the pubic bones apart. Neither of these forces, however, could explain the presence of a gas streak when the patient is erect. The symphysis pubis often becomes narrower in the erect position, suggesting that weight bearing tends to push the pubic bones together. It is therefore surprising that the gas streak rarely disappears when the patient stands. However, if the pelvis is compressed by slight manual pressure on both greater trochanters, the gas disappears from the symphysis, irrespective of whether the patient is in the erect, prone, or supine position.

It is apparent that increased intra-abdominal pressure resulting from a growing fetus does not push the pubic bones apart since the gas streaks often appear very early in pregnancy and may persist for as long as three weeks after parturition.

It is of particular interest that the gas streak disappears if the symphysis pubis widens to more than 11 mm. It seems likely that with marked separation at the symphysis there is tearing of the fibrocartilage and ligaments with obliteration of the fissures by either blood or edematous fluid. In such instances there is no longer a relative vacuum and the gas streak disappears. The necropsy evidence of Loeschcke supports this explanation. In primiparae, he found recent lacerations of the fibrocartilaginous disc during the first eight days after delivery. Hemorrhages into the fissures accompanied these lacerations.

From an anatomical consideration it is apparent that changes must also occur in the sacroiliac joints, but these changes are very difficult to demonstrate. In the current study there was no convincing evidence of a gas streak in any sacroiliac joint.

Residual osseous changes following separation during pregnancy are occasionally quite severe and may cause difficulty in differential diagnosis. This is especially true in succeeding pregnancies if pain and tenderness appear in the pubic area before a fetal skeleton is visible or before an early pregnancy is suspected. The residual roentgen changes in the pubis may simulate tuberculosis or other infection, osteitis pubis, or rheumatoid arthritis. The demineralization which occurs during pregnancy may closely resemble the resorption of the pubic bones seen occasionally in hyperparathyroidism.

SUMMARY

Roentgenograms of the pelvis of pregnant women near term revealed a streak of gas density in the symphysis pubis in 41.5 per cent. It is believed that this streak of decreased density is similar to the gas streak seen in joints of the extremities when traction is applied. Presumably the normal separation of the symphysis pubis during pregnancy results in a partial vacuum, and gas is released from the surrounding tissues into normal clefts in the fibrocartilage of the symphysis pubis.

The gas streak may appear during the first trimester but is most commonly seen during late pregnancy, and it persists for as long as three weeks after delivery. The gas streak is not present when there is a marked degree of separation of the pubic bones or marked mobility at the symphysis.

Extensive permanent roentgen changes may occur in the medial portions of the pubic bones following moderate or marked separation at the symphysis pubis during pregnancy. The most common changes are cyst-like areas of bone resorption and irregularity and sclerosis adjacent to the symphysis. The roentgen appearance may closely simulate other bone diseases.

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SUPERVOLTAGE (2,000 KILOVOLT ROENTGEN RAYS) IRRADIATION WITH A RESONANT TRANSFORMER GENERATOR*

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INTRODUCTION

INTEREST in high energy irradiation is justified in view of its increased effectiveness in the treatment of cancer. The major physical advantages of supervoltage roentgen rays are: reduced absorption in the skin and increased relative depth dose. The clinical advantages, derived from the above, are: the ability to deliver necessary tumor lethal doses to a variety of large deep-seated tumors, which could not be effectively irradiated with 250 kv. roentgen rays; and, when employing multiple portal precision crossfiring techniques or rotation therapy, the ability to deliver 6,000 to 10,000 roentgens to a localized tumor volume with little or no damage to intervening normal tissues. An additional advantage of supervoltage roentgen rays is its relatively small biological effect per incident roentgen in bone as compared with lower voltage radiation.

We will describe a General Electric 2 mev. resonant transformer generator installed at the Hospital for Joint Diseases in New York in December, 1950. A similar 1 mev. apparatus was employed by one of us[2] at Walter Reed Army Hospital since 1943.

PHYSICAL ASPECTS

There are at present three types of commercially available apparatus for the production of 2 mev. roentgen rays or equivalent radiation: the resonant transformer generator, the electrostatic generator of the Van de Graaff type,[9] and the telecurie unit using cobalt 60 as the source of gamma rays.[7] The telecurie unit has the simplest mechanism. Its low initial cost suggests that it is the most economical. However, the resonant transformer produces a roentgen flux five times greater than the cobalt unit (Table v). Therefore the resonant transformer can handle two or three times as many patients per day, unless compromises of reduced target-skin distance and percentage depth dose are accepted for the cobalt unit. As the output of the cobalt unit diminishes with time, this difference becomes further accentuated. When rotation techniques are employed, the necessary large target-skin distance further reduces the rate of tumor dose.

The resonant transformer type of 2 mev. apparatus (Fig. 1) is comparatively large in size, heavy, and requires a higher room than the electrostatic generator. These apparent economic disadvantages are compensated for by the following advantages. The resonant transformer generator has a roentgen output of 108 r per minute at 100 cm. target-skin distance, compared with 74 r/min. from the electrostatic generator. The high output of the resonant generator permits treatment of 30 patients in a seven hour day, three-fourths of the patients being treated with rotation techniques. This feature of high roentgen flux is the most important and commonly overlooked item in the selection of a supervoltage roentgen-ray apparatus. Our experience has shown that interruptions for maintenance repair seldom occur and are of a minor nature.

DESCRIPTION OF 2 MEV. RESONANT TRANSFORMER GENERATOR

The principles underlying the operation of this apparatus have been described by Charlton and Westendorp[1] in connection

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with industrial roentgenography. The apparatus consists of two series-resonant circuits tuned to 180 cycles per second, the roentgen tube being connected across the secondary inductance. The 180 cycles exciting current is supplied to the primary coil by a motor generator set. The coils are housed in a steel tank 5 feet in diameter and 8 feet long. This tank is filled with sulfur hexafluoride gas, at 60 p.s.i., which provides insulation for the high voltage circuits (Fig. 2).

The AC voltage supplied to the roentgen tube is regulated from the control panel by varying the field of the exciting generator. The peak kilovolts are adjustable from 1,000 to 2,000 kv. (peak). However, there

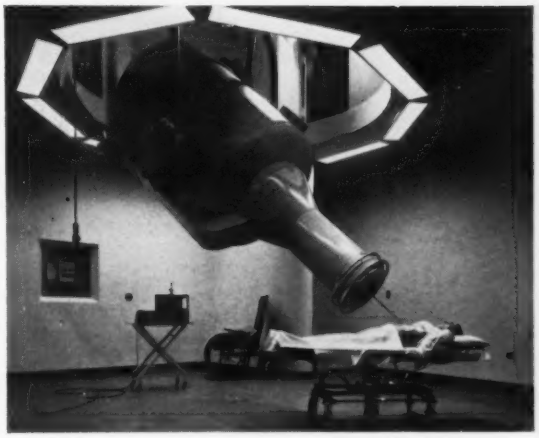

FIG. 1. The 2 mev. resonant transformer generator and mounting.

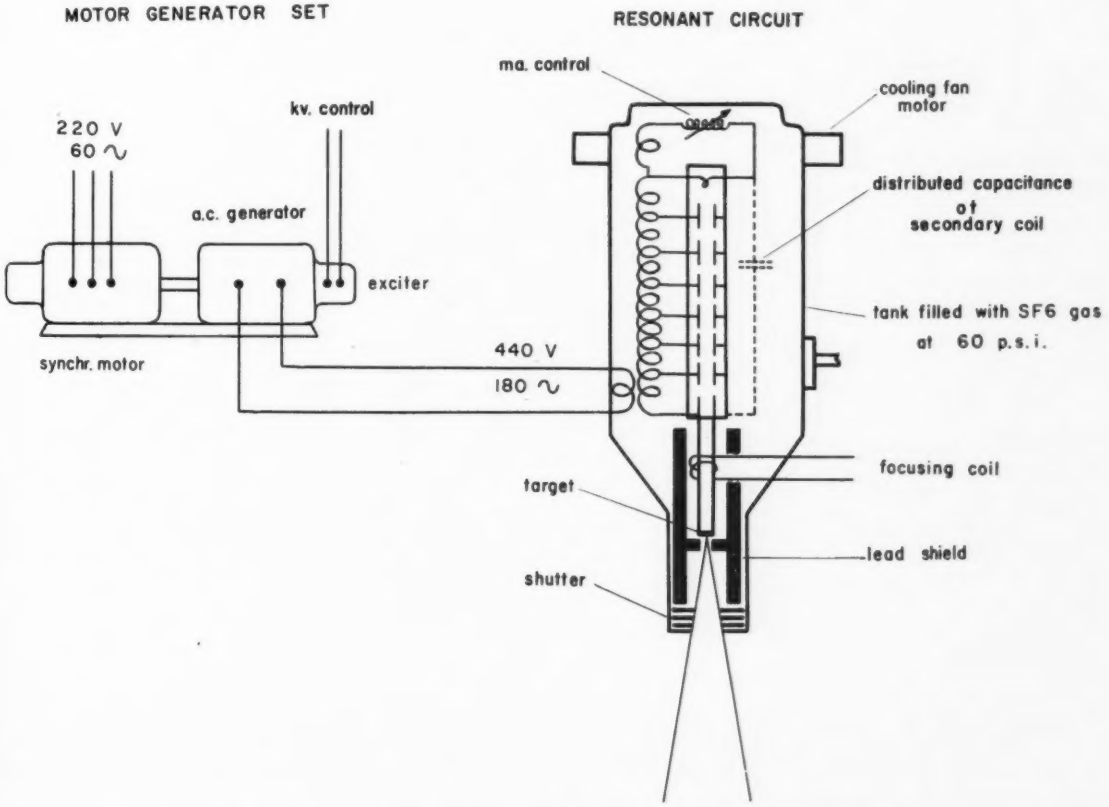

FIG. 2. Schematic diagram of 2 mev. resonant transformer generator, roentgen tube housing and power supply. The synchronous motor drives the AC generator at the proper speed to deliver 180 cycles AC at 440 volts. Inside the tank, this voltage is first multiplied approximately 200 times by the wire turns ratio of the primary and secondary coils, and is additionally multiplied due to the resonant principle. The filament is at the top of the roentgen tube. There are 20 sections to the roentgen tube over which the 2 million volts are evenly distributed. At the lower end of the tube is an extension chamber which contains the target, water cooling jacket and focusing coil. Details are shown in Figure 3.

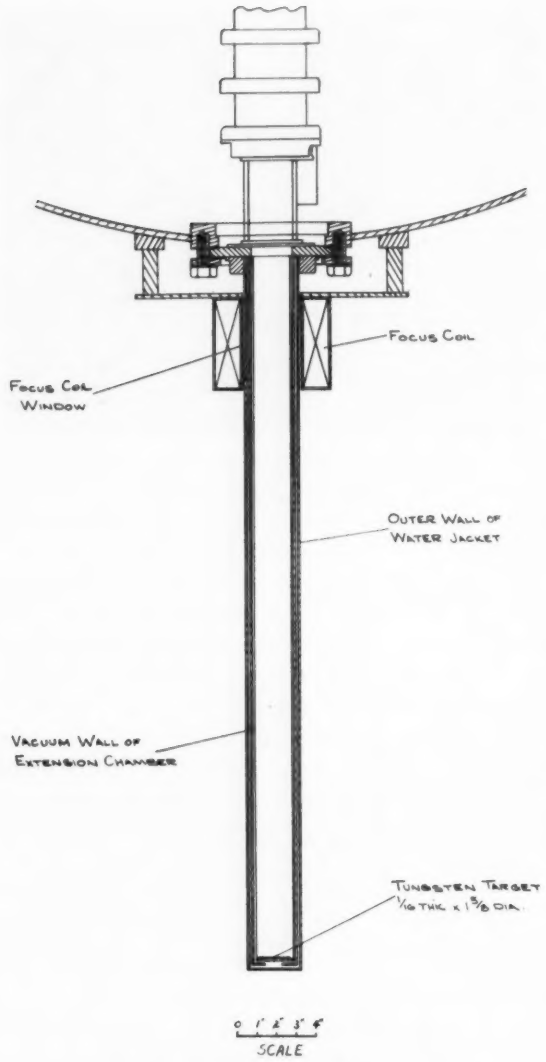

FIG. 3. Extension chamber of roentgen tube.

is little point in operating the apparatus below its maximum performance since the roentgen-ray output at these voltages increases approximately as the third power of the applied voltage.

The roentgen tube is of the multisection type and is permanently evacuated and sealed, thus requiring no pumping. The metal electrodes separating the glass sections are connected to the corresponding turns on the transformer stack by metal springs (Fig. 2) in order to obtain a constant potential drop throughout the length of the tube. Power for the filament is obtained from two turns at the high voltage end of the transformer secondary winding. The filament current is regulated by means of a reactor coil, remotely controlled from the instrument panel.

A focusing coil is located on the roentgen tube extension chamber (Fig. 2). The focusing current can be appropriately adjusted for each value of the tube voltage and current. The focal spot on the tungsten target measures approximately 1.3 cm. in diameter. At 2,000 kv. (peak) and a plate current of 1.5 ma., the output can be kept constant to 1 per cent without special precautions.

Two motors mounted inside the tank circulate the insulating gas which maintains an even temperature throughout. The anode of the tube is surrounded by a water jacket fed from a closed cooling system (Fig. 3). Sets of interlocks are provided, rendering the machine inoperative in case of failure of the cooling system, surge in the high voltage circuit which might damage the tube, and undue variation in temperature and gas pressure. If any part of the system is not functioning properly, it can be quickly identified by pilot lights on the control panel connected with the interlock circuit.

Operation of the apparatus is simple. The first morning warm-up requires twenty minutes to bring the voltage to maximum. Subsequent exposures require only thirty seconds to elevate the voltage from zero to 2 mev. No roentgen rays are emitted until approximately 1,700 kv. is reached. It then takes about ten seconds to raise the voltage to 2,000 kv. This minimal timing error is corrected in the following way: the automatic timer can be connected to the tube voltage measuring circuit so as to cut in at any predetermined voltage. In this installation it was set at 1,860 kv. (peak) for the following reason: During the time when the voltage is still rising from 1,860 to 2,000 kv. (peak), the roentgen-ray output is smaller than at full voltage This dose deficiency is compensated for by the roentgen-ray output occurring while the voltage is

rising from 1,700 to 1,860 kv. (peak), during which period the timer is not yet operating

THE MOUNTING OF THE APPARATUS

The entire unit is located in a separate wing of a three story building. The treatment room in the basement houses the tank which contains the transformer and the roentgen tube. Above this room is a well, two stories high, which houses the elevator mechanism. The space around this well on the upper floors contains the motor generator set and air conditioning equipment. The over-all height from the floor of the treatment room to the top of the well is 30 feet.

The treatment room, 29 by 23 feet, was purposely made unusually large to facilitate various activities connected with this apparatus, to permit free movement of stretchers and a treatment bed, to provide space for a rotating platform, and for auxiliary and experimental equipment. Three walls of this room are of concrete 2 feet thick, and a fourth wall, toward which the beam is pointed most of the time is 3 feet thick. Careful survey of the areas outside the room confirmed the adequacy of this protection.

The transformer tank containing the roentgen tube is mounted in a yoke suspended from a single point on the elevator mechanism. This permits the beam to be placed at any angle in any direction and at any desired height from the floor. This feature, whose value will become apparent later, considerably increases the flexibility and versatility of the apparatus.

When the roentgen tube is aligned vertically, the unit can be retracted into the well, so that the tube head clears the floor by 213 cm. When the axis is in horizontal position the beam can be lowered to a level, 109 cm. above the floor. For purposes of personnel protection, the range of rotation of the machine about its vertical axis has been limited to 120 degrees. All these motions are motor actuated and controlled by a single hand switch.

The control panel is mounted outside the treatment room. Adjacent to it, a window, 2 feet square, made of lead glass plates totalling 2 feet in thickness permits supervision of most of the treatment room.

OPERATIONAL PERFORMANCE

A unique feature of the resonant transformer circuit is its stability of operation. Interruptions seldom occur, and consist of minor adjustments in auxiliary equipment. Tube life is long. In the 1 mev. apparatus used in clinical radiation therapy, it has extended up to 4,000 hours. Our 2 mev. tube has been running for 2,575 hours until today without any signs of deterioration. This compares favorably with some Van de Graaff apparatuses for which tube lives of only a few hundred hours recently have been reported.[8,11]

DOSIMETRY

The dose distribution from a 2 mev. resonant transformer roentgen apparatus had not yet been studied. Therefore a comprehensive survey was executed by means of thimble chambers and film dosimetry. The dose distribution along the central axis was obtained with thimble chambers (see below). The contours of the isodose curves were obtained by a combination of ionization chamber and film techniques.

Thimble Chamber. The outside dimensions of the thimble chamber were 8 mm. diameter and 7 mm. length. The wall thickness is approximately 1 mm. "air equivalent" material. This chamber was calibrated against a parallel plate air chamber so that it read correctly in roentgens for 200 kv. roentgen rays. For 2 mev. roentgen rays air dosage measurements, the thimble chamber was covered with a 3 mm. thick lucite cap in order to provide radiation equilibrium. For depth dose measurements within an untempered masonite phantom (density 1.01 grams per cc.), the thimble chamber was fitted snugly into a recess inside the masonite block.

Air Dose. In Table 1, the output of this roentgen-ray unit in air for various param-

TABLE I

AIR DOSES FOR 10 BY 10 CM. FIELD

kv.	ma.	Target-Skin Distance (cm.)	Added Filter	Half-Value Layer	r/min.
2,000	1.5	100	None	5.0 mm. Pb	174
2,000	1.5	100	4 mm. Pb	7.2 mm. Pb	108
2,000	1.5	125	4 mm. Pb	7.2 mm. Pb	69

eters is listed for a 10 by 10 cm. field.

The air dose for fields other than 10 by 10 cm., are obtained by employing the factors listed in Table II. For example, with a 5 by 5 cm. field and target-skin distance of 100 cm., the dosage rate in air is $108 \times 0.96 = 103.7$ r/min.

This variation of air dose with field size is due to variation in secondary radiations from the filter and collimating system, and, in the case of small fields, to the utilization of radiations mainly from the central portion of the focal spot.

Skin Dosage. Before discussing skin dosage, it is helpful to consider in detail the processes occurring within the first few millimeters of skin and subcutaneous tissues. Figure 4*a* illustrates the secondary electron emission from successive thin layers of tissue below the skin surface. The electrons are emitted chiefly in the forward direction. In the first few millimeters, absorption of the primary roentgen-ray beam is negligible, and the photons eject a constant number of secondary electrons from each successive thin layer traversed by the beam. Let us assume that all the secondary electrons have a range of 3 mm. (This corresponds to the average range of the secondary electrons from 2 mev. roentgen rays.)

TABLE II

VARIATIONS OF AIR DOSE WITH FIELD SIZE
Dist. 100 cm.; H. V. L. 7.2 mm. Pb

4×4 cm.	5×5 cm.	7×10 cm.	10×10 cm.	15×15 cm.	20×20 cm.
0.95	0.96	0.99	1.00	1.01	1.02

The electrons emitted from the first layer penetrate up to layer No. 4 (Fig. 4*a*); those from the second and third layers penetrate up to layers No. 5 and 6 respectively. Twice as many electrons traverse layer No. 2 as layer No. 1. The electron flux increases in the successive layers up to layer No. 4. Electrons passing through the fourth layer are contributed from layers No. 4, 3, and 2, but not fro mlayer No. 1. Conse-

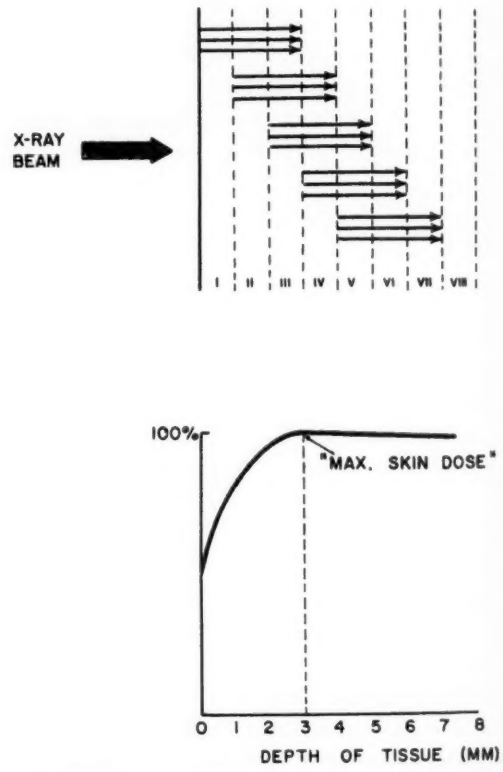

FIG. 4. (*a*) Illustration of secondary electron emission in successive thin layers of tissue below the skin surface. (*b*) Dose distribution versus depth in the superficial layers of the skin.

Table III

BACKSCATTERING FACTORS FOR VARIOUS FIELD SIZES

4×4 cm.	5×5 cm.	7×10 cm.	10×10 cm.	15×15 cm.	20×20 cm.
1.01	1.01	1.02	1.02	1.03	1.04

quently full electron equilibrium is established 3 mm. below the surface of the skin.

The results of this discussion are summarized in Figure 4*b*, which shows a curve of dose due to the secondary electrons versus depth in the superficial tissue layers. The electron flux rises to a maximum at 3 mm. depth, which corresponds to the average range of the secondary electrons. It then decreases slowly due to the absorption of the primary roentgen-ray beam and the inverse square law effect. The maximum point of this curve is called the *maximum skin dose*. This maximum skin dose represents a stable reference point, since it is easy to measure the dose rate at this point.

Obviously the *skin surface dose* is smaller than the *maximum skin dose*. This is confirmed by the clinical observation that supervoltage radiation produces mild early skin reactions. However, the late skin effects are severe, due to the intense ionization and consequent fibrosis in the deeper layers of the skin, at the level of the maximum skin dose. Therefore, physically and clinically, the maximum skin dose is a desirable reference point, and is used to express the surface dose for 2 million volt roentgen rays.*

* The true dose at the surface of the skin varies from 40 per cent to 80 per cent of the maximum skin dose, depending on several factors such as: the amount of air in the intervening distance between the target and the skin surface, electron emission from the collimating device, atmospheric conditions, and field size.

Table IV

2000 KV. (PEAK) DEPTH DOSE DATA

Physical Constants: T. S. D.: 100 cm.
Added filtration: 4 mm. lead
H. V. L.: 7.2 mm. lead*

Depth (cm.)	Per Cent Depth Doses					
	Field size (cm.)					
	4×4	5×5	7×10	10×10	15×15	20×20
0.3	100	100	100	100	100	100
1	96	97.5	99	99	99	99
2	92	94	96	96	96	96
3	88	90	92	92	92	92
4	81	83	86	87	88	88
5	74	76.5	80	81	83	83
6	69	70.5	74	75.5	79	79
7	63	65	69	70	74	74
8	58	60	65	66	70	70
9	53	55	60	61	65	66
10	49	51	56	57.5	61	62
12	41	43	48	49	53	55
15	32	33.7	38	39.5	43	46
17	27	28.5	33	34	37.5	41
20	21	22.5	25	27	30	34
22	18	19	21	23.5	26	30.5
25	14	15	17	19	21	25.5

* The half-value layer depends not only on the voltage and filtration but also on other factors, such as field size and the amount of scattered radiation reaching the ionization chamber. The given half-value layer of 7.2 mm. lead actually ranged between 6.8 and 8 mm. lead. The depth dose tables, given above, are the only "true" measure of quality.

TABLE V

COMPARISON OF ROENTGEN OUTPUT AND 10 CM. DEPTH DOSE DATA OF COMMERCIALLY AVAILABLE SUPERVOLTAGE THERAPY UNITS

	r/min. (air) at 100 cm. T.S.D.	Per Cent Depth Dose for Different Field Sizes at 10 cm. Depth		
		5×5	10×10	20×20
1 mev. resonant transformer[1]	84	41	52	58
Cobalt 60 teletherapy unit[2]	22	53	58	62.5
2 mev. electrostatic generator[3]	74	53.4	57.2	—
2 mev. resonant transformer[4]	108	51	57.5	62

[1] Physical Foundations of Radiology. Second edition. Paul B. Hoeber, New York, 1952. Also see bibliographic ref. 1.
[2] Johns, H. E., *et al. Brit. J. Radiol.*, 1952, *25*, 302–308.
[3] Trump, J. G., *et al.* Personal communication.
[4] The authors.

The Backscattering Factor and Maximum Skin Dose. For supervoltage radiation the backscattering factor is a small correction (Table III) which is applied to the *air dose* in order to obtain the maximum skin dose. This backscattering factor refers specifically to the *maximum skin dose* and not to the surface dose, as in the case of lower voltage roentgen rays.

To measure the maximum skin dose, the thimble is half imbedded in the surface of the phantom, and the unimbedded half covered with a lucite cap 3 mm. thick. This effectively brings the center of the chamber to the point of maximum intensity while it is also in secondary electron equilibrium.

Depth Dose Data. Measurements were made with the thimble chamber along the central axis of the beam. Table IV gives the conventional depth dose data using 100 per cent as the maximum skin dose at 0.3 cm. depth.

To aid in the comparison of supervoltage apparatuses of similar half-value layers, Table V has been prepared. It shows the roentgen flux at 100 cm. distance and the percentage depth doses at 10 cm. depth for three different field sizes.

The greatest difference between these various types of apparatus lies in their roentgen output. The cobalt 60 teletherapy unit has a low output of 22 r/min., as compared with 108 r/min. from the 2 mev. resonant transformer apparatus.

Although the electrostatic generator operates at 2 million volts *constant potential*, and the resonant transformer at 2 million volts *peak*, there is no significant difference in the percentage depth doses, due to the heavy added filtration (4 mm. Pb) in the latter machine.

Isodose Curves. Isodose curves were first constructed for a few field sizes by using a thimble chamber. This method has many disadvantages. It is a time-consuming procedure. The relatively large chamber provides poor resolution, especially at the edges of the beam where sharp gradients in intensity occur. Within the energy range under consideration, the blackening of an irradiated roentgen film provides a reasonably accurate indication of dose distribution.[5,6] The procedure ultimately employed was to use the ionization chamber for absolute dosage measurements along the central axis of the beam, and film densitometry to plot the complete isodose curves.

A special densitometer assembly was designed (Fig. 5). It consisted of a Welch

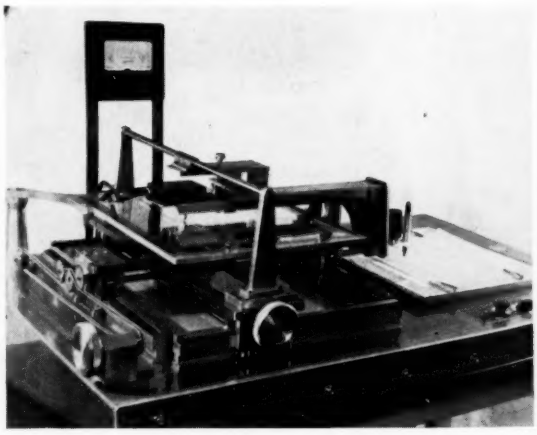

FIG. 5. Densitometer assembly for photographic isodose determinations.

densitometer head firmly mounted on two moveable arms so as to permit scanning of the entire exposed film, while simultaneously plotting the isodose curve. Several isodose curves are reproduced in Figures *6a*, *6b*, *6c*, *6d*, *6e* and *6f*. Figures *6a*, *6b* and *6c* are the conventional isodose curves for roentgen-ray beams incident perpendicularly to the skin. They are similar to those published for the 2 mev. electrostatic generator.[10] Figures *6d*, *6e* and *6f* show the distortion of the isodose curves occurring when the beam enters the skin at various angles.

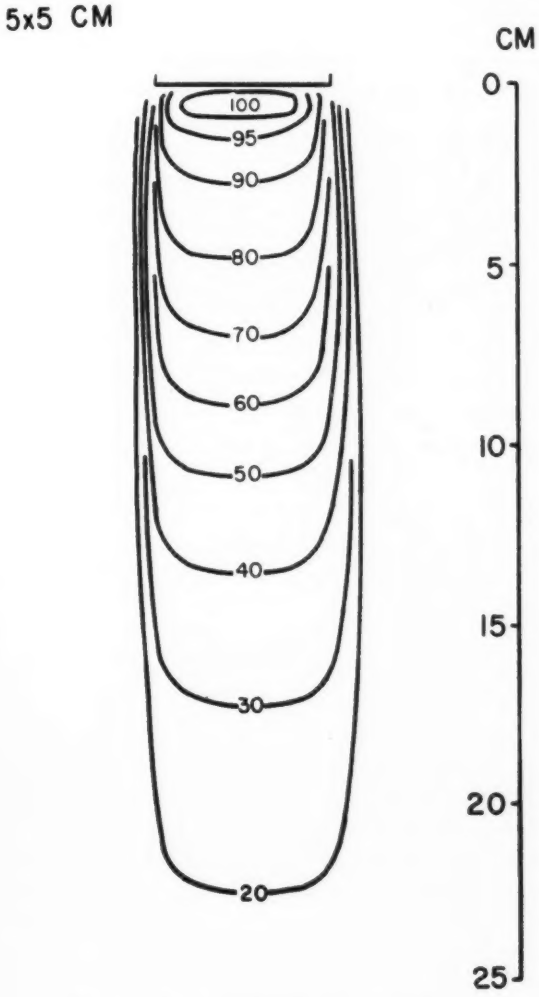

Fig. *6a*. Isodose distribution for 5 by 5 cm. field.

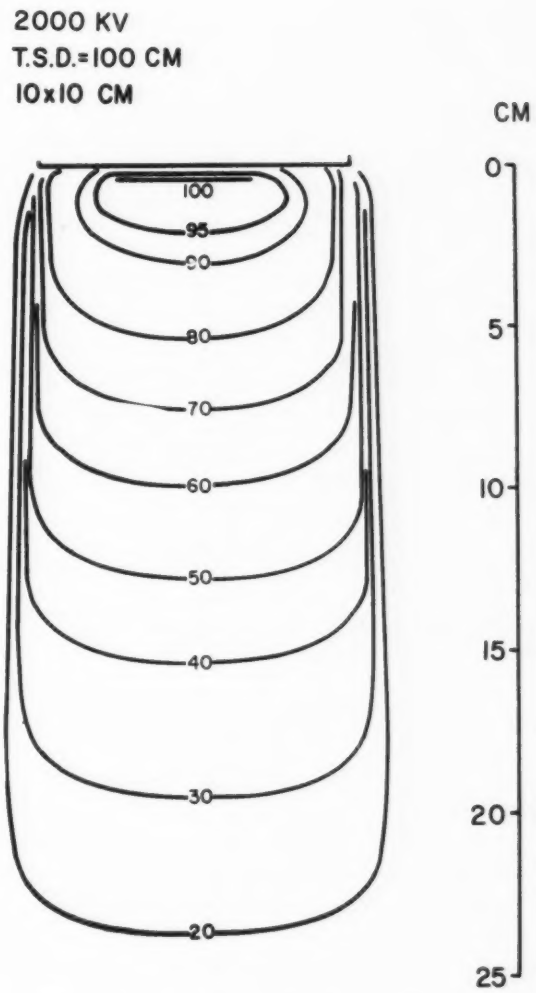

Fig. *6b*. Isodose distribution for 10 by 10 cm. field.

FIELD LOCALIZATION

The size of the rectangular roentgen-ray field on the skin is controlled by a shutter constructed of intermeshing 3/4 inch plates totalling 3 inches (7.5 cm.) of lead. Each side of the rectangle has four plates. These lead plates are bevelled so as to have minimum penumbra with an 8 by 8 cm. field, which is the median size field employed. The intermeshing construction is more advantageous than single lead blocks because less of the scattered radiation emitted from the shutter can reach the skin.

The fields are positioned on the patient by means of a light beam which is obtained

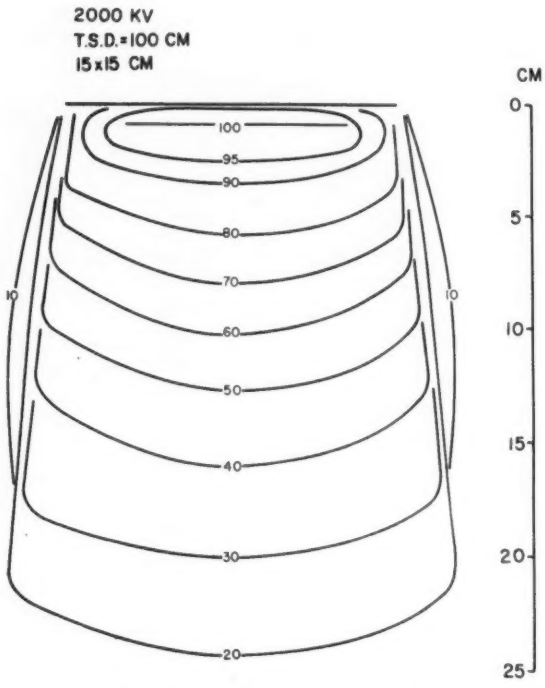

Fig. 6*c*. Isodose distribution for 15 by 15 cm. field.

through a 45° mirror from a projection lamp within the tube head (Fig. 7). The light beam will coincide with the roentgen-ray field only if the light source appears to be located at the focal spot of the tube (Fig. 7*a*). With large focal-skin distances a small error in the position of the filament of the light bulb will cause an appreciable error in the location of the light field (Fig. 7*b*). As the filament ages, it will stretch, change shape, and move out of position. It must therefore be checked periodically. This is done photographically by putting lead markers on the edge of the light field (Fig. 7*b*). The film is then exposed to the roentgen-ray beam. The lead markers should coincide with the edge of the roentgen-ray field if the light beam is properly adjusted (Fig. 7*a*).

DIAPHRAGMS AND GRIDS

Circular and irregularly shaped fields were obtained by employing accessory devices mounted in front of the tube head.

The function of a grid with 250 kv. radiation is to deliver large quantities of radiation through the skin in pencil beams to minimize skin damage. Homogeneity in the depth is approached as a result of lateral scattering, diversion of the beam, and slight variations in beam angulation from day to day. With supervoltage radiation, there is no necessity for skin-sparing devices. Supervoltage grid technique therefore provides the facility for studying indirect effects of radiation on tissues not traversed by the pencil beams of radiation. Consequently the beams must be sharply defined, with minimal penumbra, and the direction of the beam must be accurately reproduced with each treatment.

The construction of an adequate grid is

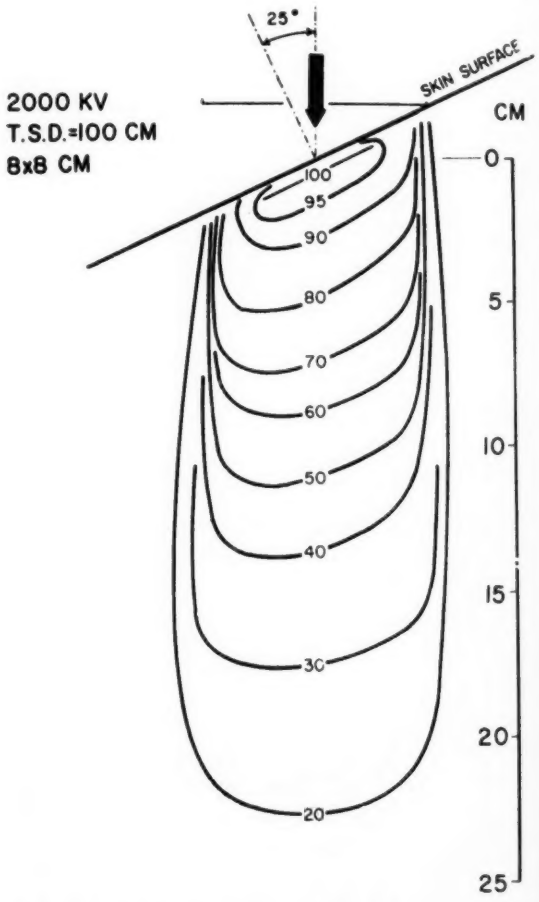

Fig. 6*d*. Isodose distribution for an 8 by 8 cm. field incident at a 25° angle from the normal. The target-skin distance is measured along the central axis of the beam.

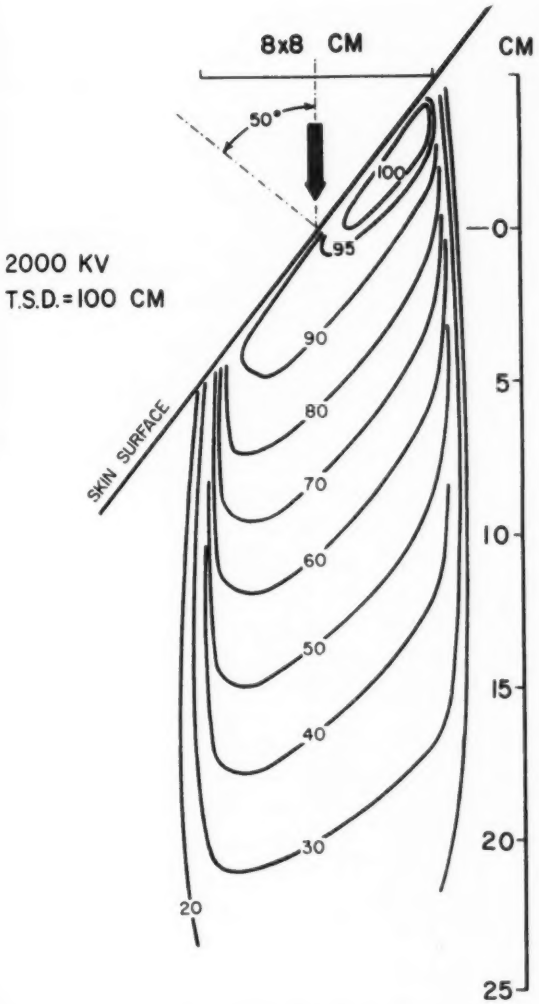

FIG. 6e. Isodose distribution for an 8 by 8 cm. field incident at a 50° angle from the normal. The target-skin distance is measured along the central axis of the beam.

complicated. For best definition of each pencil beam and for accurate reproduction of each treatment, the grid should be situated about 20 cm. from the patient. The large area of the grid and its thickness (2 inches of lead) results in a heavy device. Each hole must be drilled parallel to the rays of a diverging beam, otherwise there results pencil beams of different configurations (Fig. 8). The secondary electron emission at a distance of 20 cm. from the grid was investigated by film methods and found to be negligible.

EVALUATION OF FUNDAMENTAL PRINCIPLES OF SUPERVOLTAGE RADIATION THERAPY

The physical advantages of supervoltage radiation (reduced skin effect and increased depth dose) makes possible the administration of tumor doses considerably higher than 4,000 r to deeply seated and subsurface lesions. This could rarely be achieved with 250 kv. roentgen rays. The high percentage depth dose readily permits administration of optimum average daily tumor doses of 225 r to 275 r or more with

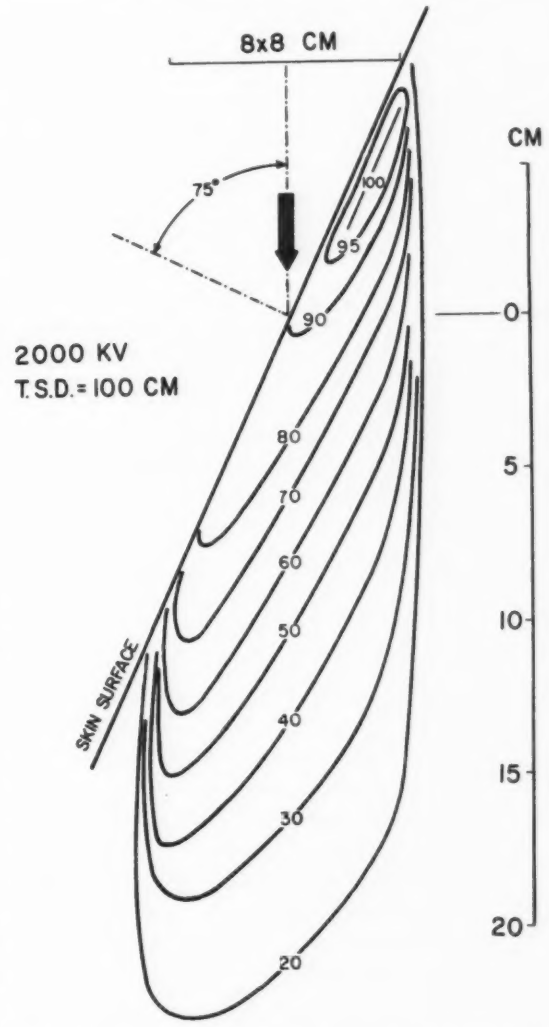

FIG. 6f. Isodose distribution for an 8 by 8 cm. field incident at a 75° angle from the normal. The target-skin distance is measured along the central axis of the beam.

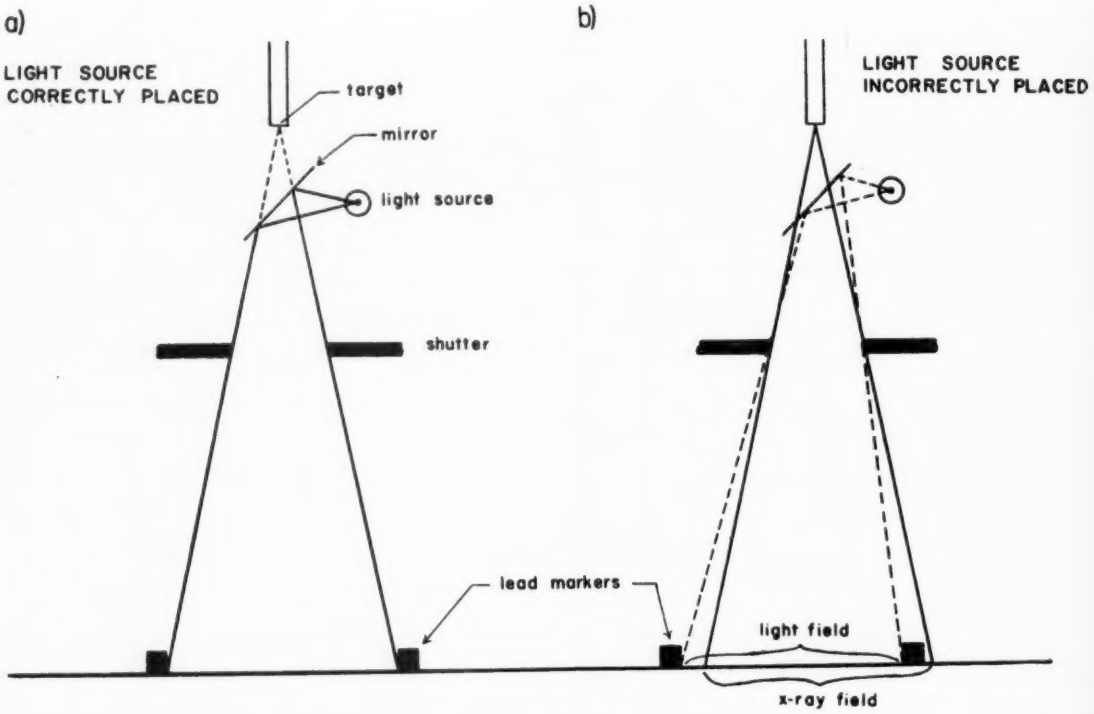

Fig. 7. Operation of light beam localizer. (*a*) Correctly adjusted. Light field coincides with roentgen-ray field. (*b*) Filament of light source in incorrect position. Therefore the roentgen-ray field and light field do not coincide.

relatively small volume dose effects.* In order to achieve total tumor doses of 6,000 r to 9,000 r within twenty-one to twenty-eight days, supervoltage radiation is required. However, unless the radiation is properly administered, severe and fatal damage to normal tissues will occur.

Single Portal Technique. The radiotherapist surveys an isodose curve, and observing the low skin absorption and high percentage dose, is tempted to deliver the total tumor lethal dose through a single portal. The early mild skin reaction seems to corroborate this decision. However, after a time, disastrous clinical complications ensue. The early mild skin surface erythema is gradually replaced by a dense block of fibrous tissue, 2 to 5 cm. thick. This contracts and distorts the skin; immobilizes adjacent structures (spinal column or other bone); induces radiation osteogenic sarcoma; or if the maximum surface dose

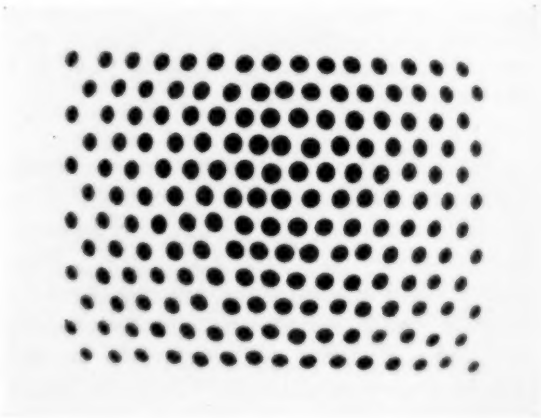

Fig. 8. Roentgenogram of 8 by 10 cm. field through a 5 cm. thick lead grid. Since the holes in the lead block are all parallel to the central axis of the roentgen-ray beam, considerable distortion occurs at the edges of the field.

* The range of optimum tumor dose expressed herein is derived from clinical studies of fractionation techniques corroborated by serial biopsy studies, chiefly of squamous cell epithelioma. It represents the summated opinion of that school of radiotherapy which believes that the optimum "over-all time" is twenty-one to twenty-eight days.

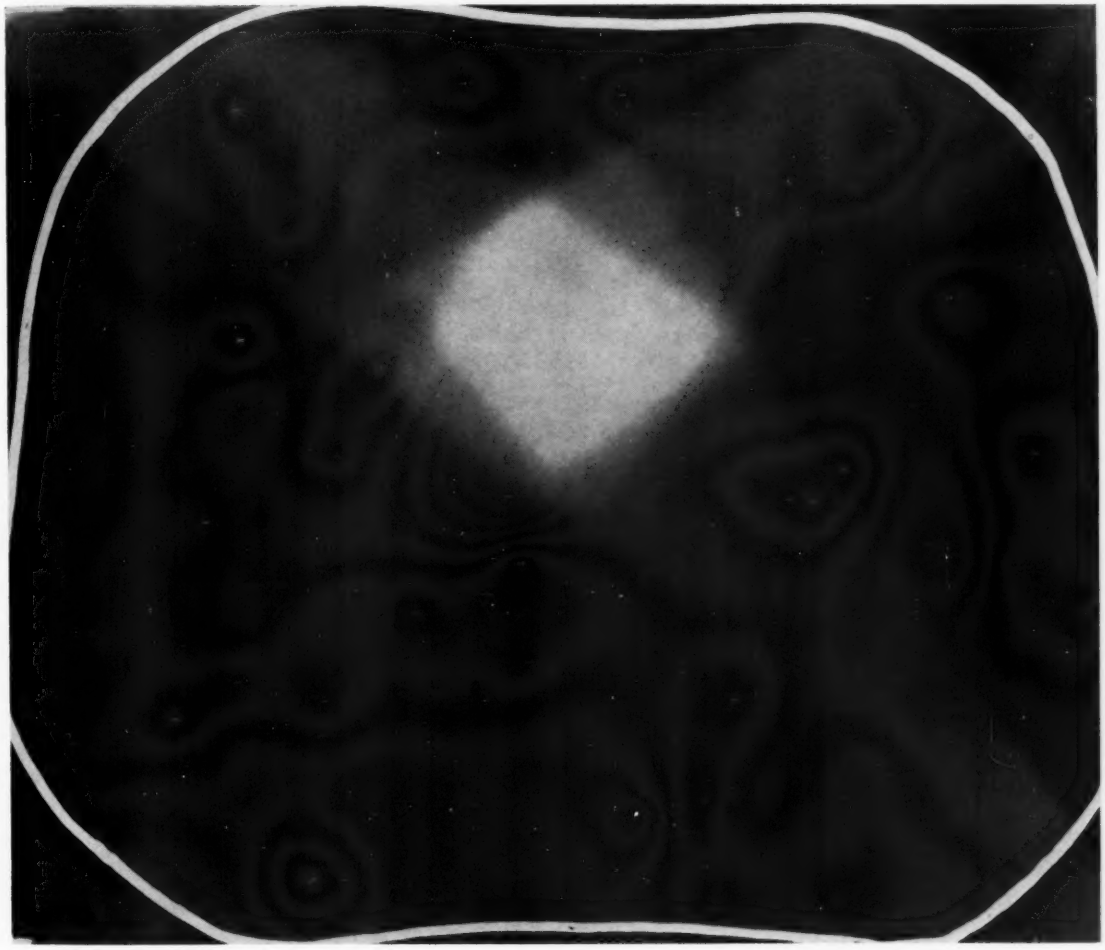

Fig. 9. Dose distribution in a chest phantom using four 5 by 5 cm. fields aimed at one point. The beams were angulated so that the exit area would not overlap the incident portal. In spite of precision aiming, which was more accurate than obtainable in clinical practice, the uneven dose distribution through the irradiated volume is apparent.

is large, will in a few years, become ischemic and slough away, leaving a deep crater.

For example, when employing the single portal, massive dose technique with 250 kv. roentgen rays to irradiate a carcinoma of the tonsil,[4] the maximum skin tolerance dose is 8,000 r in thirty-five days. The tumor dose at 4 cm. depth will be approximately 5,600 r. The severe skin reaction will reach a third degree intensity. With supervoltage roentgen rays, a comparable maximum skin dose will deliver a more fruitful tumor dose of 6,800 r. The early skin reaction is a deceptively mild first degree erythema which rapidly heals. However, after a time, severe radiofibrotic and radionecrotic effects will manifest themselves, due to the fact that not only did the tumor receive a high dose, but all the normal tissues intervening between the skin and the tumor were heavily irradiated. Therefore the primitive technique of applying large doses of supervoltage radiation through a single portal should be avoided, except for special situations.

Opposing Portals Technique. The same difficulties are present when using two opposing portals to irradiate a tumor near the center of the body (*i.e.*, retroperitoneal

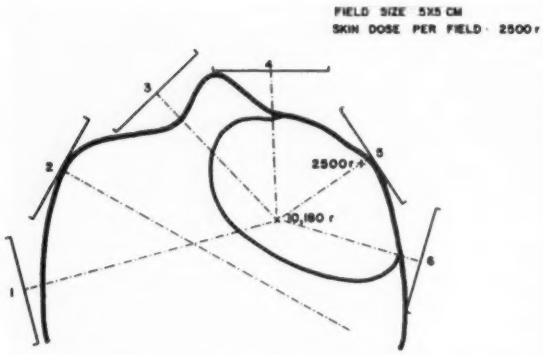

FIG. 10. Tumor of the maxillary antrum treated through six portals of 5 cm. wide fields. With the exception of portal No. 2 all beams were aimed toward one point in the tumor. The area covered by portals No. 2 and 6 lies partly outside the tumor area to cover a region of suspected tumor extension. The nonhomogeneity of dose distribution resulted in a subcutaneous recurrence at portal No. 5.

nodes from a testis tumor). This technique produces a solid column of radiation of fairly uniform intensity from front to back. In a series of tumors of the testis where maximum skin and tumor doses of 4,000 to 5,000 r in fifty to seventy days had been employed, producing only a mild transient erythema, there resulted a wide variety of severe radiation injuries: ulceration of the stomach, occasionally with perforation; ulceration of the intestines occasionally with perforation; atrophy of the kidney; and severe pneumonitis.[3] In spite of these injuries, the five year arrest rates were much higher than hitherto obtained for carcinoma of the testis. However, with improved techniques these injuries can be minimized or avoided (see below).

There are two exceptional groups where the "two opposing field technique" may be successfully employed. The first group consists of radiosensitive tumors like seminoma and lymphoma, where the total tumor dose and volume dose are much below normal tissue tolerance; and extensive disease, such as carcinoma of the ovary, primary advanced or metastatic carcinoma of the lung, wherein a large volume of normal tissue is palliatively irradiated with total tissue doses just below the tolerance level of normal tissues. The second group consists of radioresistant tumors of very large size extending from the anterior to the posterior skin surface, such as massive retroperitoneal sarcoma filling one-half the abdomen, or a large sarcoma involving the entire cross section of an extremity; and some primary advanced carcinomas of the upper lobe of the lung. To these, large tumor doses of 6,000 r to 8,000 r may be delivered because the vulnerable normal tissues have been displaced outside the beam of radiation, or else a portion of an organ (*i.e.*, upper lobe of lung) can be sacrificed without danger.

Multiple Portals. The full benefit of supervoltage radiation can only be realized by using more elaborate techniques in the form of multiple portals or rotation therapy. Multiple portal techniques with 200 kv. roentgen rays have been adequately described. With supervoltage radiation these techniques must be refined. This entails small field size and extremely accurate aiming of the beam. Figure 9 was obtained with a phantom irradiated through four portals in such fashion that the incident beam would not overlap an exit beam. The beam was aimed with higher precision than can be obtained in clinical practice. Even under these ideal conditions the non-

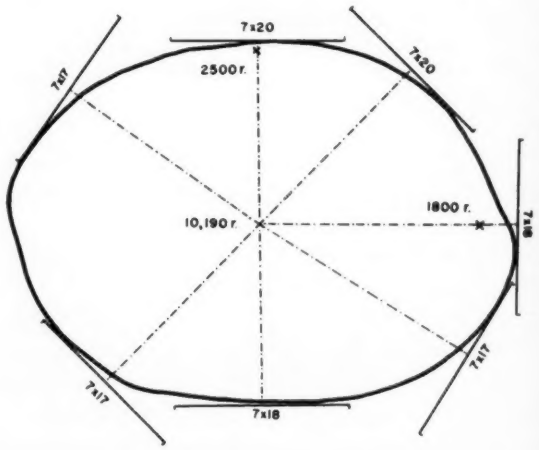

FIG. 11. Postamputation recurrent sarcoma involving the entire stump of the thigh, treated by seven fields aimed at the center. This pattern, though suitable for 250 kv. roentgen rays, resulted in marked inhomogeneity of dose distribution when 2 mev. was employed.

uniformity of the irradiated tumor volume is obvious. The addition of more portals would remedy the deficiency. However, in actual practice, the required precision can rarely be obtained. In addition, this procedure is time consuming.

The difficulties of achieving homogeneous tumor irradiation are aggravated when the tumor extends close to or lies near the skin. Figure 10 illustrates a tumor of the maxillary antrum. The pattern of the skin fields was dictated by previous experience with 250 kv. radiation. Instead of achieving reasonably homogeneous dose distribution with 2 mev., the remotest portion of the tumor received four times the dose as that of the subcutaneous portion. This resulted in a recurrent nodule in the subcutaneous region only. This error can easily be avoided by using rotation technique. Another example (Fig. 11) illustrates a massive post-amputation recurrent sarcoma in the stump of a thigh. Using seven contiguous portals girdling the thigh, a central tumor dose of 10,000 r was given in forty-nine days. Several months later, two recurrent *subcutaneous* nodules appeared at points where the tumor dose was subsequently calculated to be less than 3,000 r. Thereafter, using rotation therapy, a tumor dose of 6,000 r in forty-eight days was given to the entire stump. There was no recurrence or necrosis for one year when the patient died of metastasis. On re-evaluation of this problem, it was realized that two opposing portals would have been more efficient than multiple portals in providing homogeneous dose distribution.

Rotation. Rotation technique with supervoltage radiation provides the most homogeneous dose distribution in a tumor-bearing area, with minimal dosage to surrounding normal tissues and minimal volume dose. With proper equipment great accuracy in positioning of the patient and calculation of dose distribution is most easily achieved.

Rotation techniques will be discussed in detail in a forthcoming paper.

CONCLUSIONS

1. The resonant transformer generator is an efficient supervoltage radiation apparatus. Its large size and initial investment are more than compensated for by its high roentgen output and low maintenance cost. Its stability and reliable performance result in rare interruptions and continuity of operation. Tube life is unusually long.

2. Clinical evaluation based on nine years of experience with supervoltage radiation therapy leads to the opinion that rotation techniques utilize the advantages of supervoltage to the fullest extent. Multiple portal techniques are somewhat less efficient. The two opposing portals technique has limited indications and a high incidence of radiation damage. A single portal technique should rarely be employed.

3. With supervoltage radiation, one cannot apply the philosophy of radiation therapy based on the experience accumulated with 250 kv. New treatment concepts have been designed.

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Vol. 73, No. 3

A SYSTEM OF RADIUM DISTRIBUTION FOR TREATMENT OF CANCER OF THE CORPUS UTERI*

By R. KENNETH LOEFFLER, M.D.†
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THE dosage system for intracavitary radium treatment of cancer of the corpus uteri presented here is designed to give a predetermined distribution and intensity of radiation by the use of standard combinations of radium applicators. Even though intracavitary radium seems to have much to offer in the management of this disease, no treatment plans are available which are simple, flexible and reproducible, and which give desirable distributions of radiation. This is in contrast to the several excellent techniques in common use for cancer of the cervix.

Many writers express their radium dosage only in terms of milligram hours.[1,2,8,10,12,13] This statement of total exposure does not define the doses to the various structures within the pelvis, values necessary for subsequent evaluation of the effects of treatment. In the method described by Tod a tandem of radium tubes is used varying in number with the depth of the uterus. The exposure time is adjusted to give 5,000 r to Point A during each of two applications of about forty-eight hours, separated by a five day interval.[9] Radium tubes in tandem in the uterine canal with one ovoid at the cervix will give a fusiform distribution of radiation, neither conforming to nor taking advantage of the anatomy of the uterus and vagina. The alternative distribution, using two ovoids of half-strength in the fornices, will not greatly change the radiation contour. Leucutia describes a system based primarily on the tandem applicator, giving dosage both in milligram hours and in roentgens to different pelvic structures.[7] Heyman's technique would seem to be preferable,[2,4,5] since his distribution tends to conform to the shape of the uterus, and tables are available to give a post-calculated estimate of the dose to the outside wall of the uterus. However, a predictable and dependable distribution will not result from simply packing the uterus to capacity, nor is the shape of the isodose distribution around the uterus resulting from such packing completely satisfactory. The system described by Hurdon is expressed in terms of milligram hours, but it approaches most closely to giving a desirable dosage pattern.[6] This system requires the use of sources of different strengths in a variety of applicators, and tends to rely heavily upon the applicators in the cornua to obtain a satisfactory isodose contour. Thus, while several of the existing systems for the placement of radium within the body of the uterus have merit, none of them gives an easily reproducible, advantageous distribution of radiation.

Published series of cases by Taylor,[13] Arneson,[2] Miller[8] and Stearns[12] tend to show improved five year survival rates following treatment by radium and hysterectomy, as compared with hysterectomy alone, although this conclusion has been disputed.[11] The explanation for any improved survival resulting from preoperative irradiation of an organ which is then removed *in toto* requires some consideration. Possibilities which have been suggested are that the uterus serves merely as a depot for radium to irradiate tissues beyond the subsequent operative field, that fibrosis of small blood vessels and lymphatics will inhibit the spread of metastases at the time of surgery, and that cancer cells within the operative field are rendered nonviable so that they will not survive even if they are disseminated at the time

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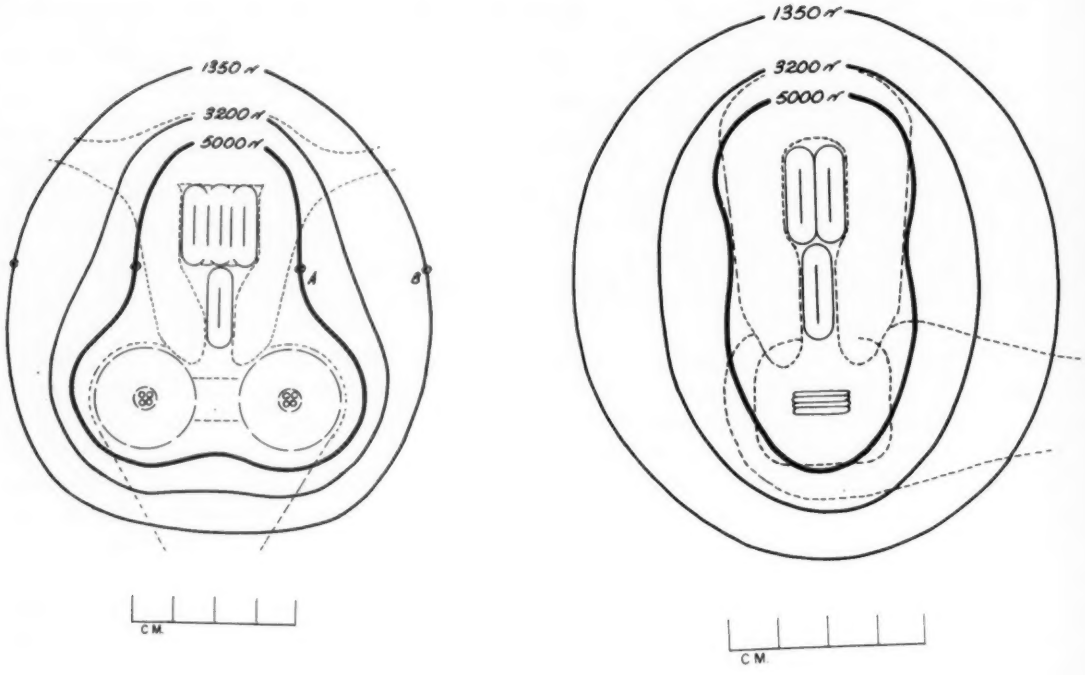


FIG. 1

of operation. Regardless of the explanation, the intent of treatment should be to "project" the radiation as far as possible, without delivering an excessive dose to the bladder, rectum or small intestine. Simultaneously, an adequate dose should be delivered to the upper vagina, since a high percentage of recurrences occur in this area.[3]

With simplicity and flexibility as primary criteria, and with a desire to utilize existing equipment, No. 0.5 Heyman applicators were adopted for positioning the uterine radium sources, in combination with the Manchester ovoids for the vaginal sources. A modified Ernst applicator can also be used for the vaginal sources and lowest uterine source.

Pending long term follow up of treated patients, it is necessary to adopt a standard dose more or less arbitrarily. The value of 5,000 milligram hours is commonly encountered in the literature.[1,3,7,10,12] This exposure from radium randomly placed in an average sized uterus is likely to deliver 6,000 to 8,000 gamma roentgens to the outer wall of the uterus. To provide a common reference point for dosage statement, the Manchester Point A was chosen because it represents a sensitive area in the pelvis, corresponds roughly to the outer wall of the uterus, and is already in common usage for expressing dosage in gynecological cancer therapy. We chose to deliver 5,000 r in thirty-eight hours to Point A, approximately two-thirds of the dose to come from the uterine sources, and one-third from those in the vagina. While 7,000 r in seven days tends to be a rather standard value for radium treatment of limited volumes, it would be impracticable to attempt to leave radium applicators in a uterus for seven days continuously. To increase the intensity and decrease the elapsed time requires some consideration of the time-dosage relationship. Most of the quantitative studies on this subject have been on the effect of roentgen radiation on skin, and the correlation to gamma radiation on pelvic structures is not direct. Again more or less arbitrarily, we have accepted 5,000 r in thirty-eight hours as ap-

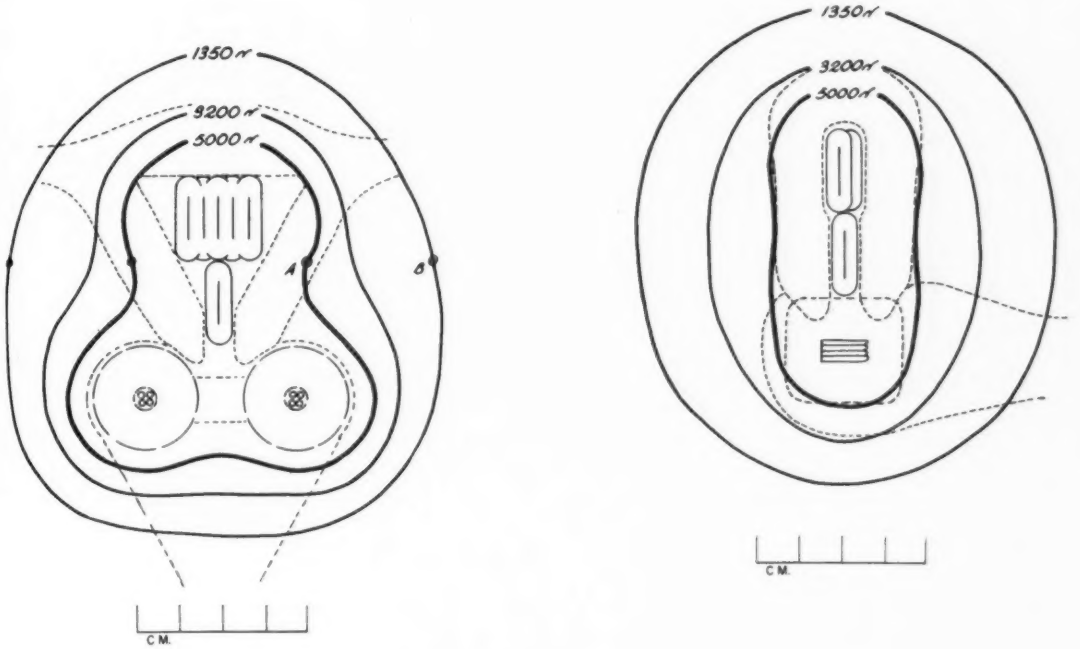


FIG. 2

proximating the biologic effectiveness of 7,000 r in seven days.

Figures 1 through 8 show schematic drawings of uteri of several sizes sectioned through the principal and sagittal planes to demonstrate the ideal distribution of

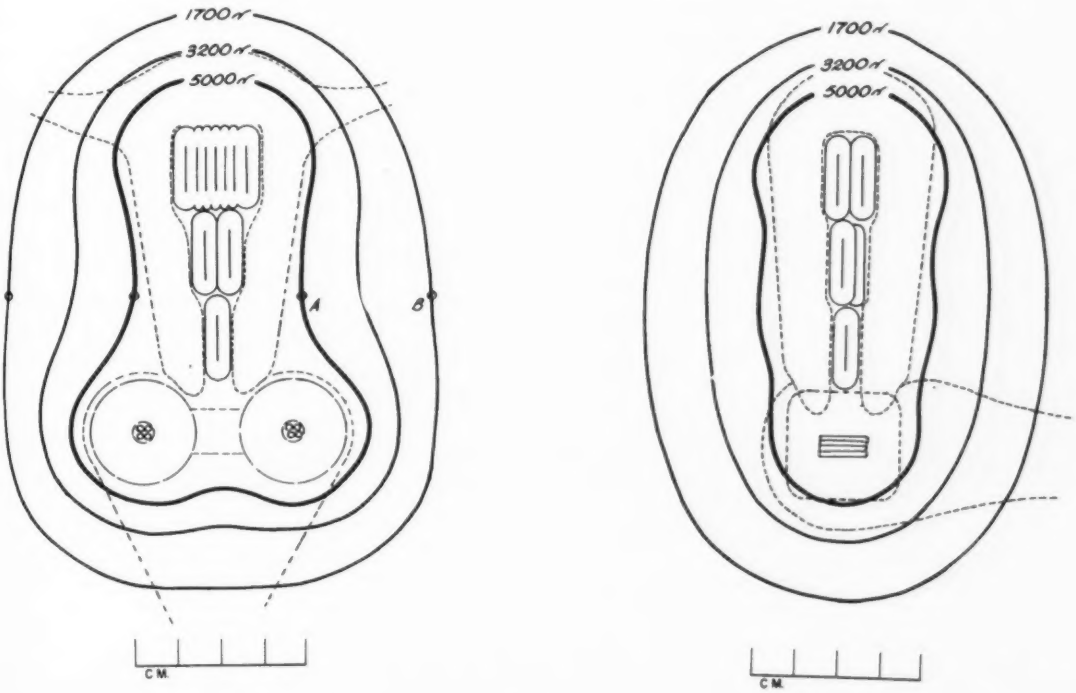


FIG. 3

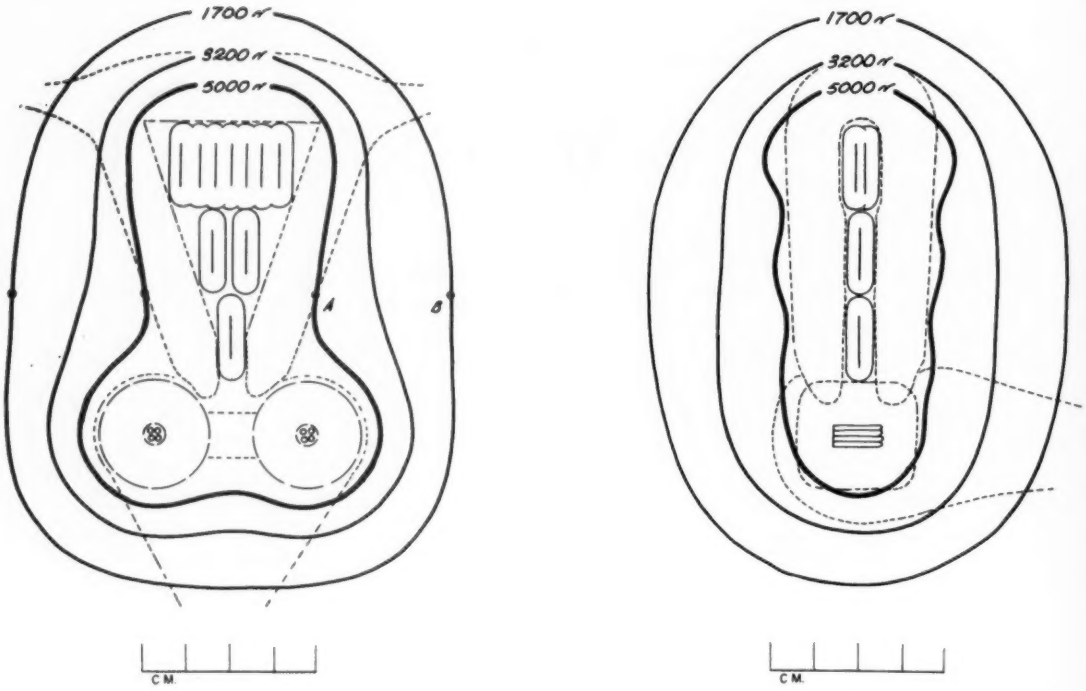
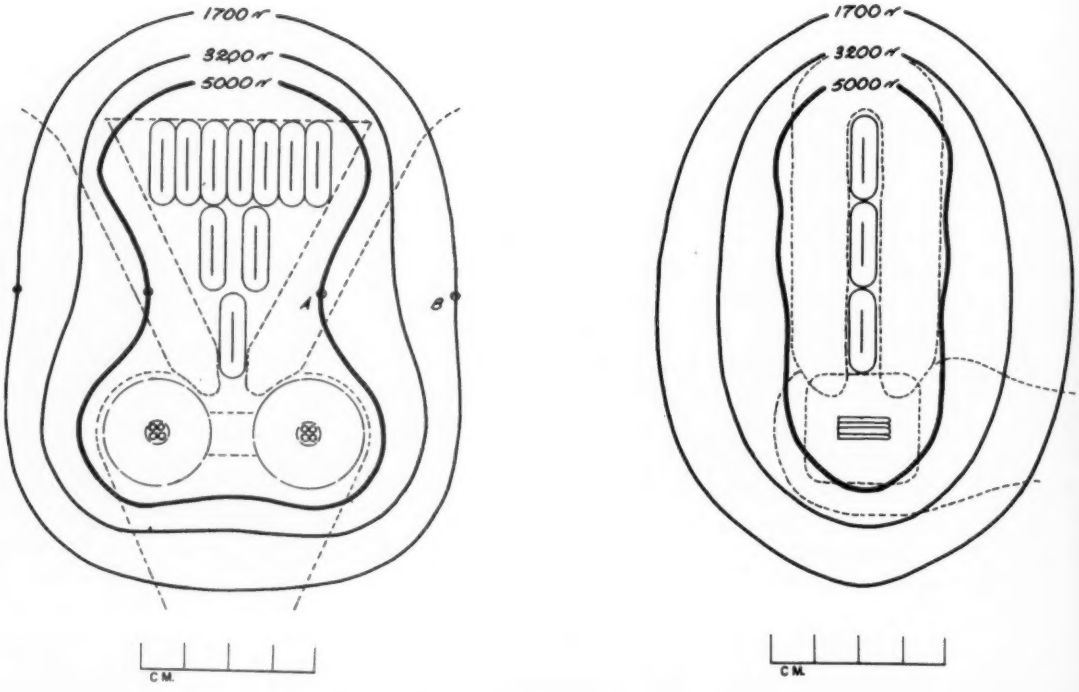

1700 m
3200 m
5000 m
A
B
C.M.
1700 m
3200 m
5000 m
C.M.

Fig. 4


1700 m
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C.M.

Fig. 5

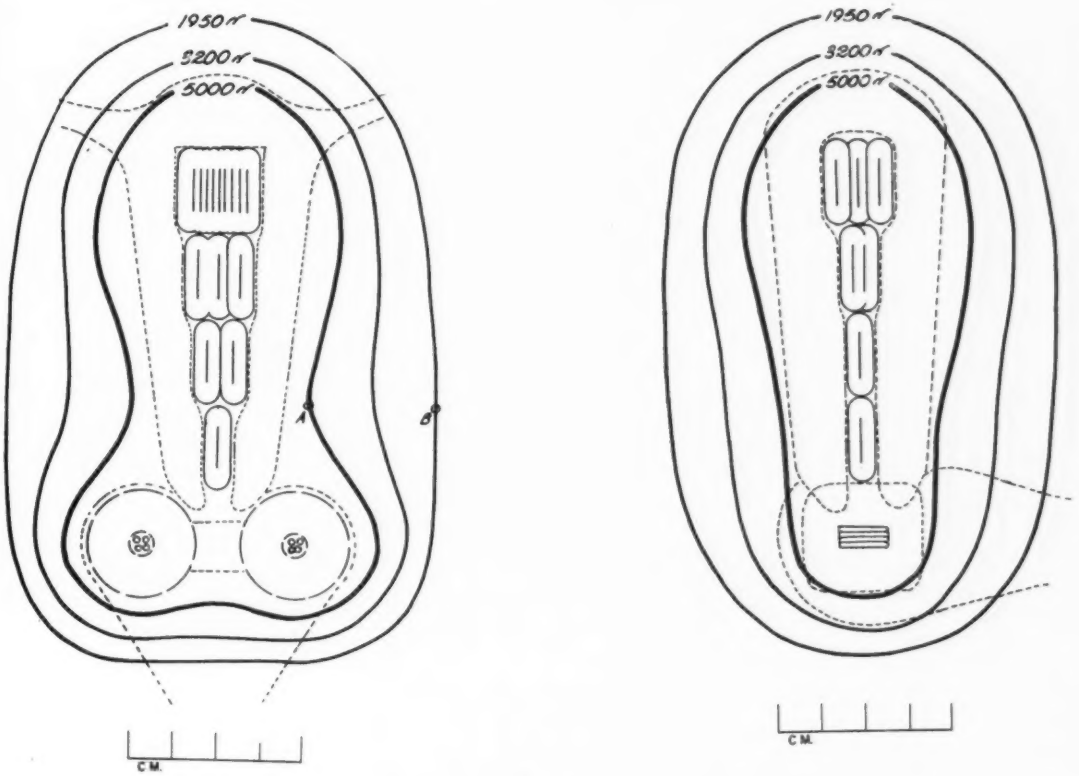
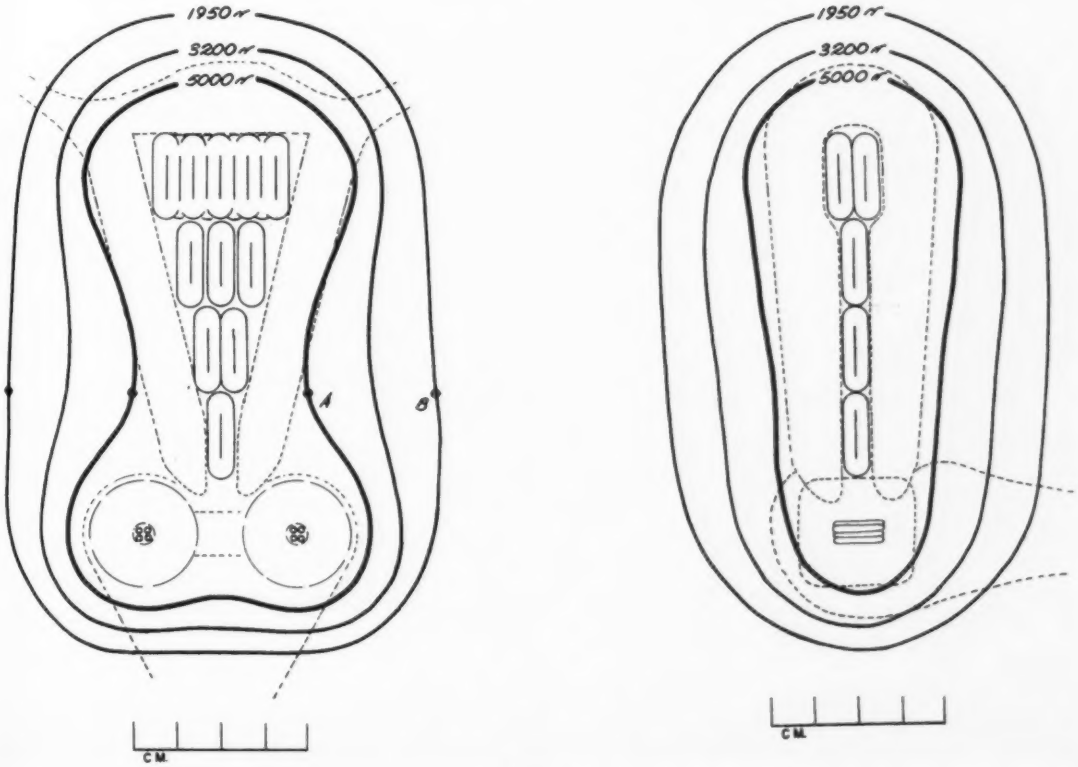

1950 r
3200 r
5000 r
A
B
CM.
1950 r
3200 r
5000 r
CM.

FIG. 6


1950 r
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B
CM.
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5000 r
CM.

FIG. 7

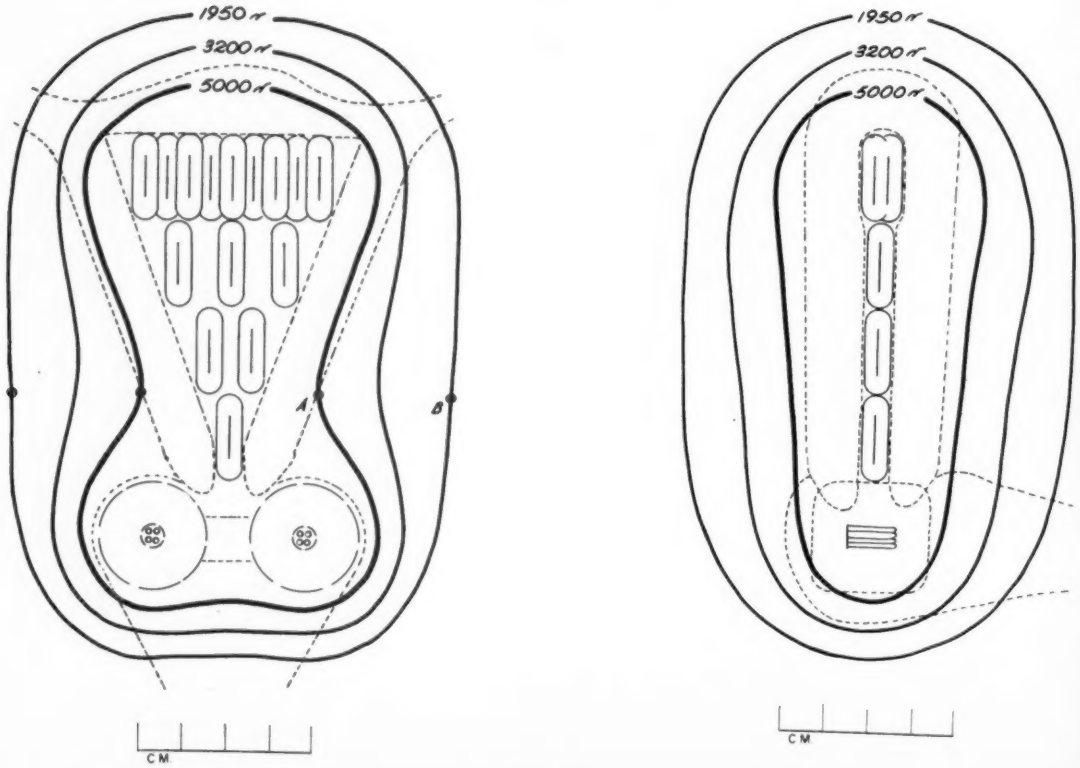

Fig. 8

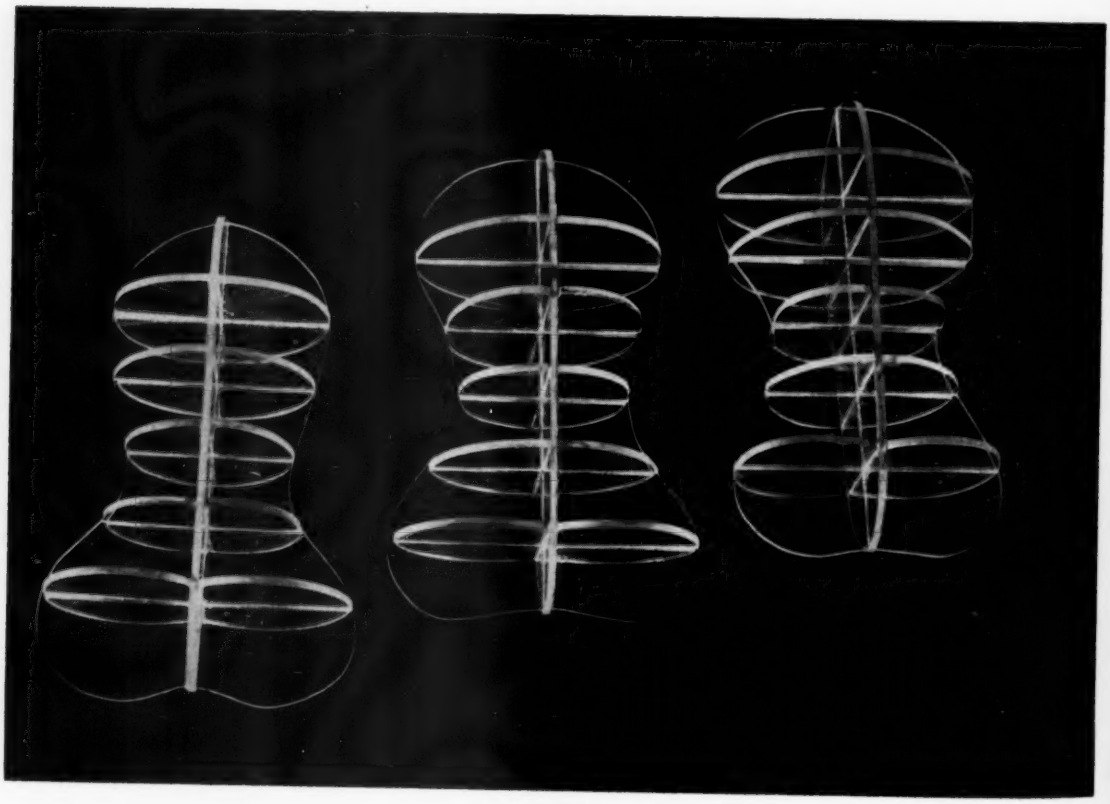

Fig. 9

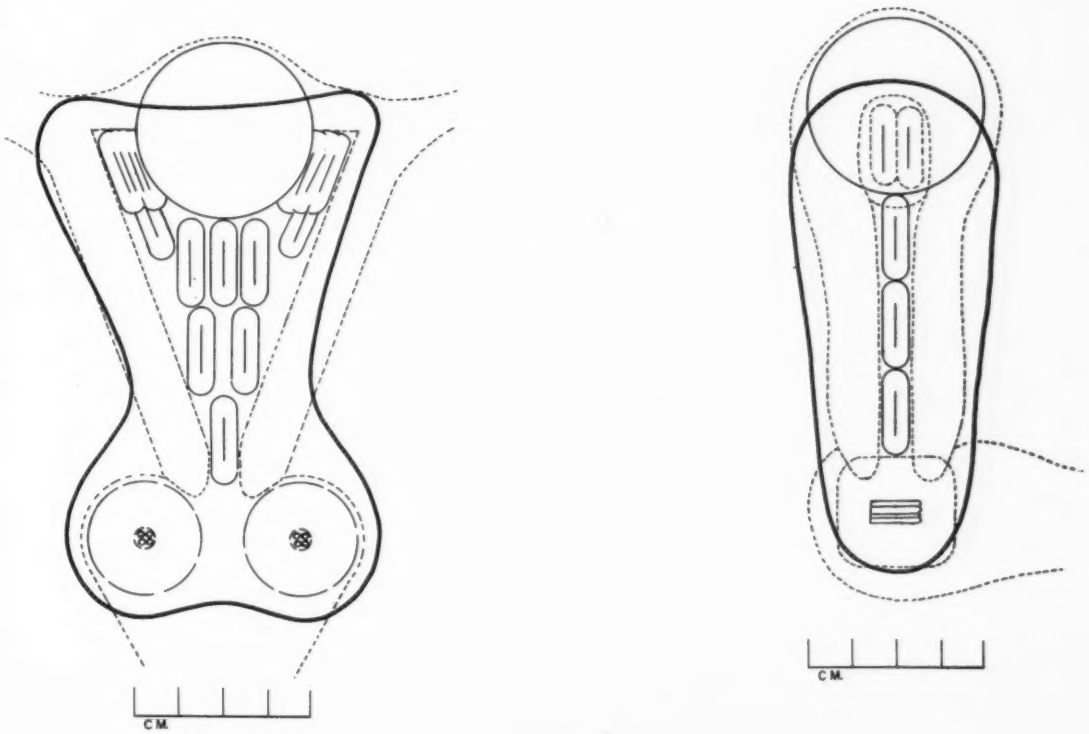

FIG. 10

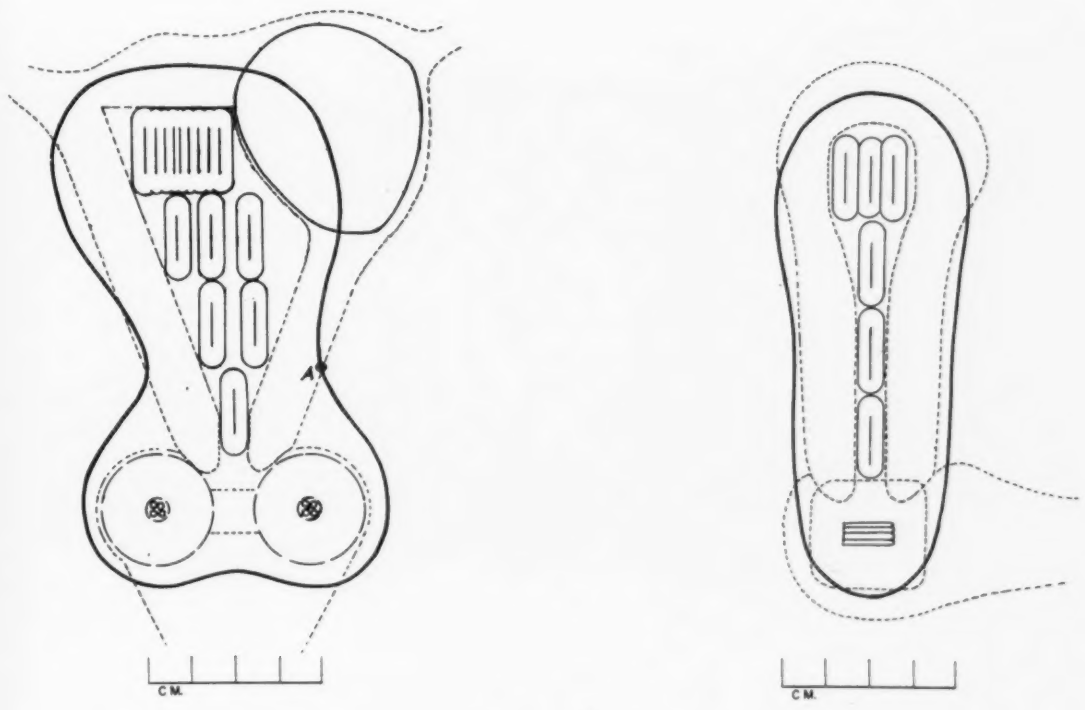

FIG. 11

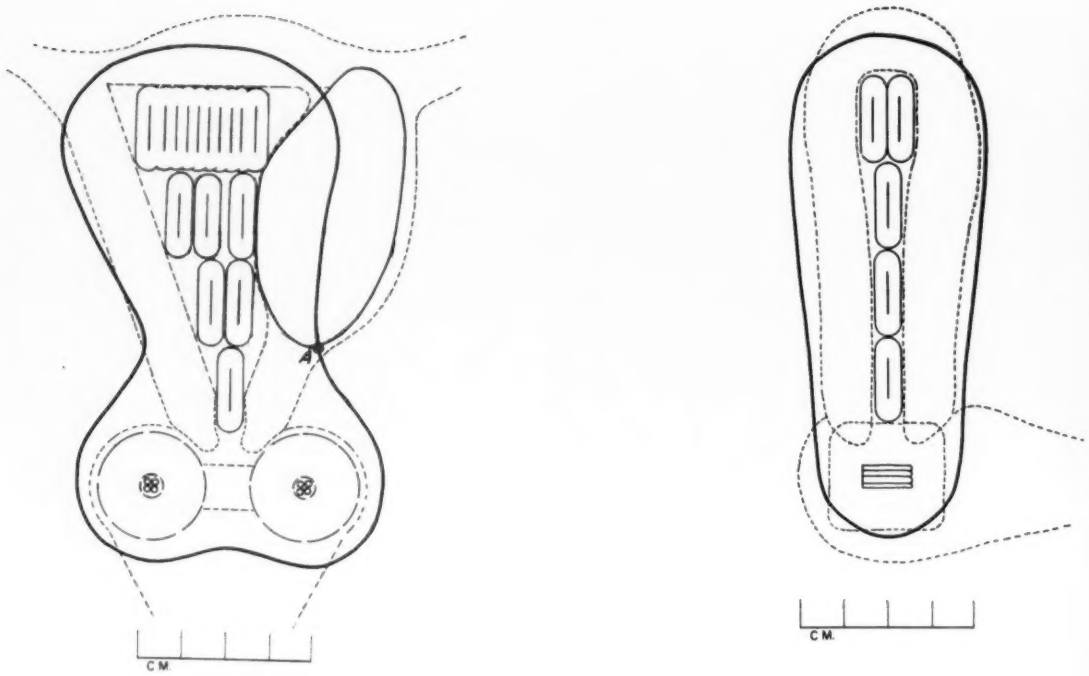

Fig. 12

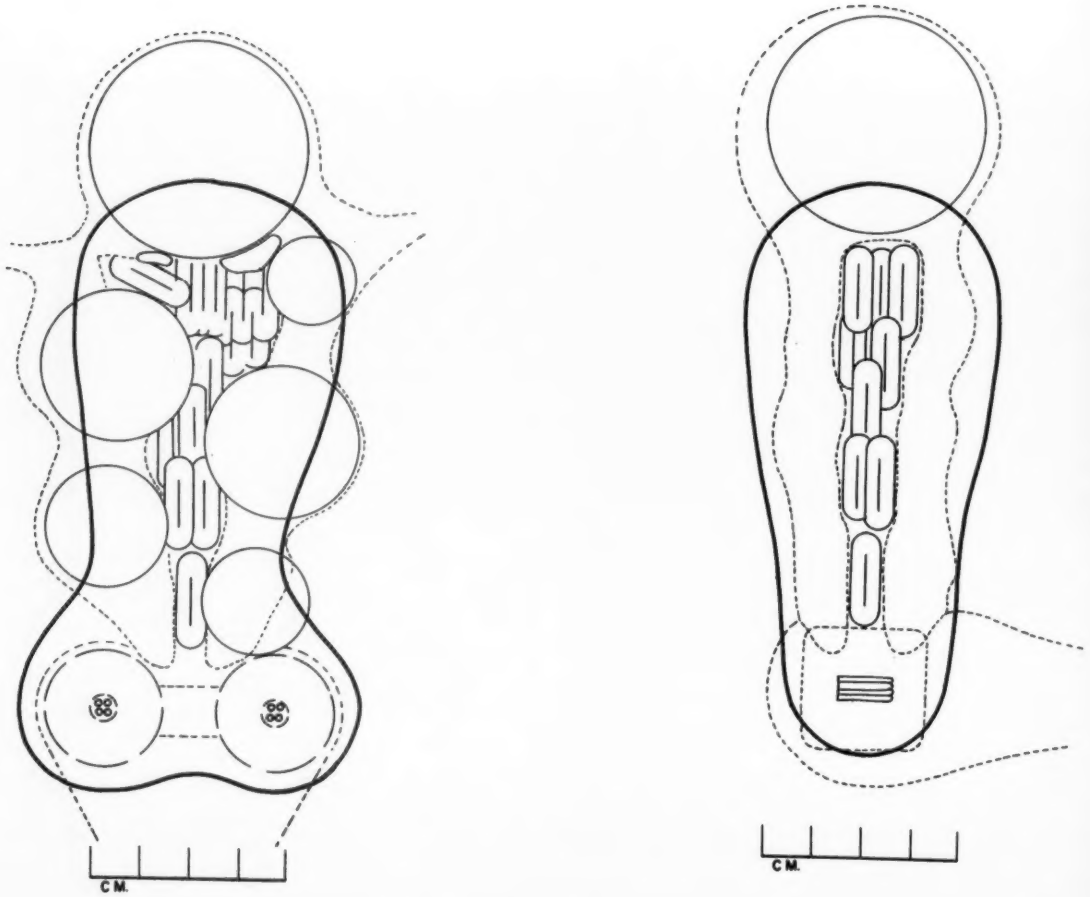

Fig. 13

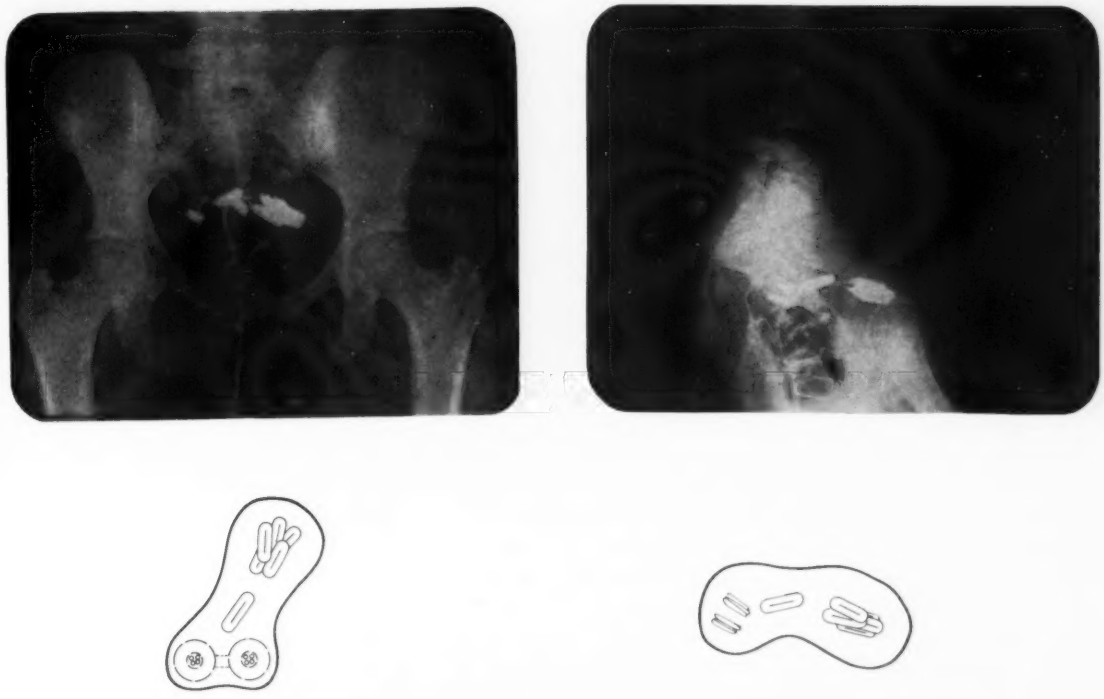

Fig. 14

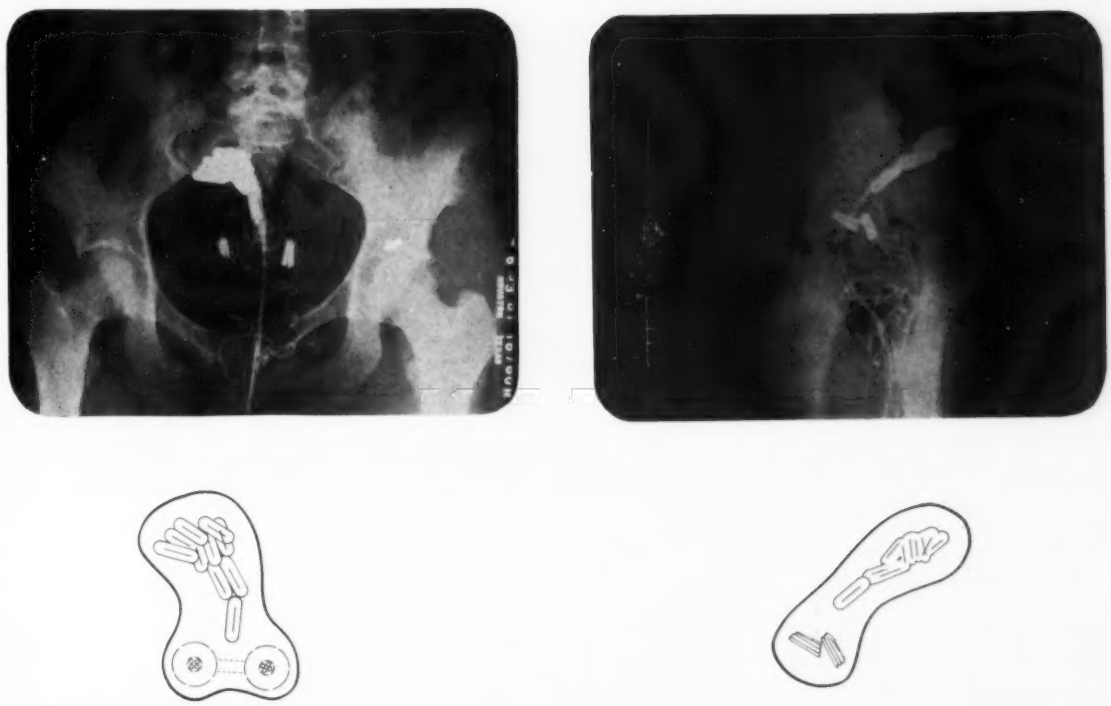

Fig. 15

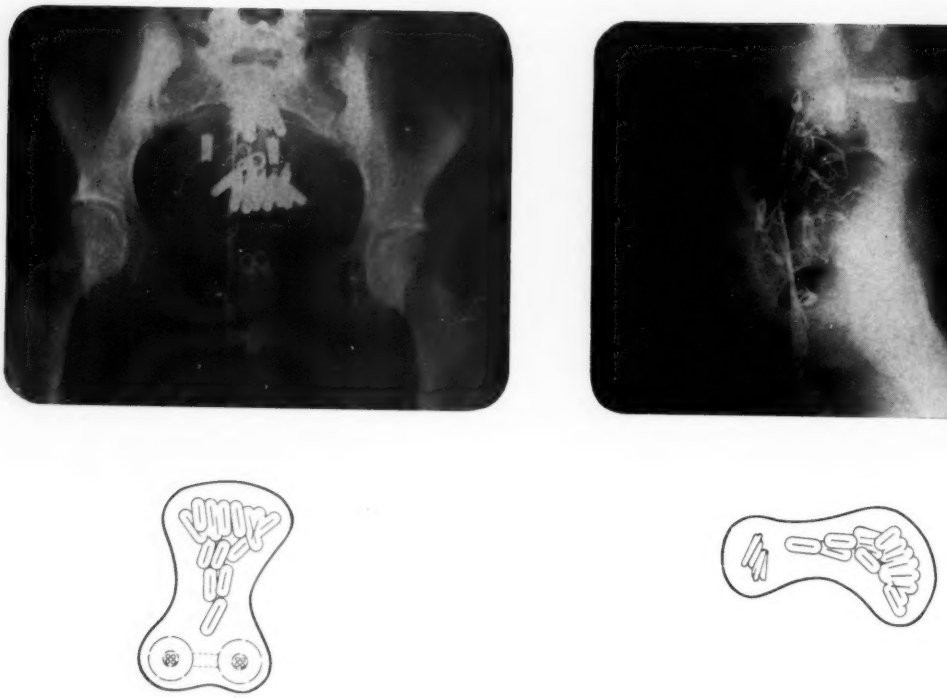

Fig. 16

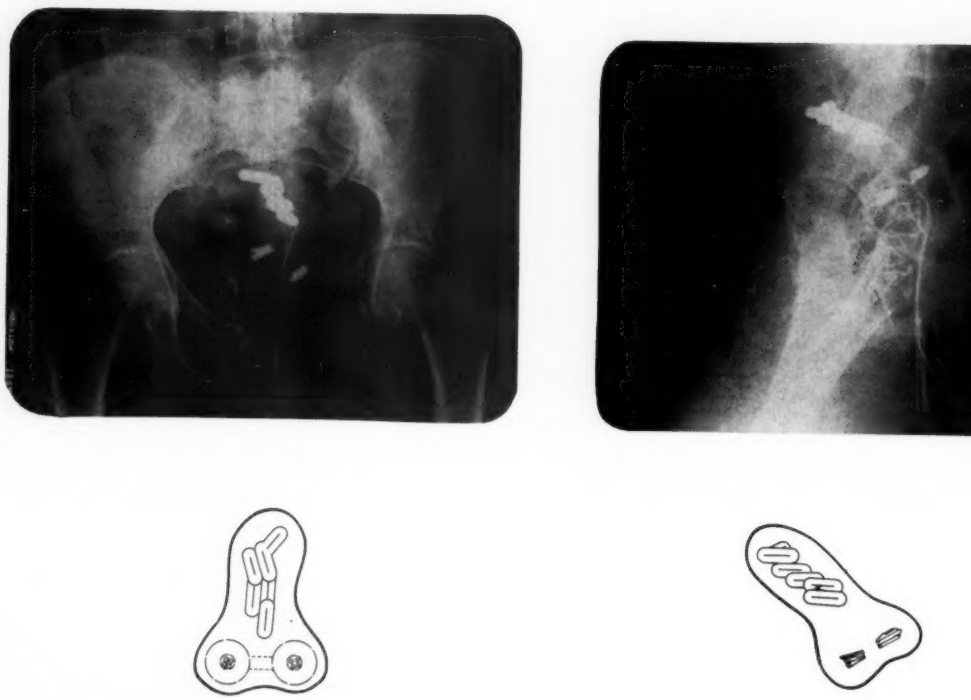

Fig. 17

the radium units, along with the resulting isodose contours.

Since uteri will rarely vary much beyond a range of 4 to 8 centimeters in depth, the distributions for shallow, medium, and deep uteri are respectively, 5-1, 7-2-1, and 9-3-2-1, in radium units. The vaginal sources conform to the Manchester system for cervix of three units in small, four units in medium, and five units in large ovoids. Any combination of these intrauterine and vaginal distributions using units of 10 milligrams of radium filtered by 0.5 mm. of platinum, will result in a dose of 5,000 r plus or minus 10 per cent in thirty-eight hours to Point A, and will give a satisfactory isodose contour. The range of dosage in milligram hours will be from 4,560 mg. hr. with small uterus and vagina, to 9,500 mg. hr. with large uterus and vagina. Despite this variation the dose is constant at Point A. The exposure in terms of milligram hours exceeds the average reported in the literature, but the increase is largely due to the vaginal sources.

As shown, the number of intrauterine sources is altered only in relation to the depth of the uterus. While more uniform contours would be obtained if the number of units at the upper level were increased for a wide uterine canal, and decreased for a narrow canal, the change is not sufficient to justify the increased complexity (Fig. 9).

Figures 10 through 13 show the isodose contours in the principal plane resulting from likely positioning of radium in the presence of bulky lesions in the upper and middle portions of the uterus.

Figures 14 through 17 are roentgenograms of the arrangement achieved in several patients, along with the 5,000 r/38 hour isodose line in the principal and sagittal planes.

CONCLUSIONS

The expression of radium exposure in milligram hours does not permit a satisfactory correlation of dose and effect. It is difficult to compare the different techniques which are in use because the exposure in milligram hours varies widely, and distribution of radium sources is not usually according to a fixed pattern. The system of radium distribution described permits the delivery of a constant dose to a volume of predictable size and shape by a simple and flexible arrangement of radium sources. It is not anticipated that this modification of existing treatment, which is necessarily local in effect, will appreciably improve the best survival rates now being realized. It is likely that with any type of therapy offering adequate control of local disease, survival will be largely dependent upon the dissemination of metastases before treatment is instituted, and upon the growth rate of the individual cancer. The positive value expected of this system is a better understanding of the effects on tumor and adjacent normal tissues when related to dose, time, and distribution of radiation. It should be possible to minimize recurrences or complications when they are due to unsuspected areas receiving inadequate or excessive doses.

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The author takes this opportunity to express his thanks to Dr. Vincent P. Collins for his many suggestions and support and to Dr. R. T. Reinke for his valuable help in the preparation of this paper.

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DISCUSSION

Dr. Alfred I. Sherman, St. Louis, Missouri. The use of intrauterine radium for the treatment of endometrial carcinoma is well established. For the inoperable cases it is the treatment most advocated, and for the operable cases has been proved to be very effective as a preoperative procedure in certain types of endometrial cancer. Sterilization of the uterine tumor preoperatively has been shown to improve the prognosis markedly. There is no doubt that the results obtained will vary directly with the adequacy of the irradiation. If one is to improve upon the results of irradiation in this disease more effective means of irradiation are necessary. Because of gross enlargements, irregularities of the cavity and associated fibroids, as well as differences in location, size and extent of the lesions, the intrauterine application of radium presents many difficulties. A system which would give a uniform cancerocidal dose of radiation to the pelvis without over-irradiation of rectum and bladder is desirable.

Dr. Loeffler reviews the many published techniques and draws the same conclusion as did Heyman, Arneson, Nolan and many others, that multiple capsule packing technique is the preferable procedure.

The author is to be commended for his tendency to disregard milligram hours of total exposure and to define dosage in roentgens delivered to special points in the pelvis.

His attempt to set up a distribution of radium to give constant dosages to a specified point, regardless of the uterine configuration, is an excellent step forward in the improvement of radiation results for the treatment of endometrial carcinoma. The roentgenograms demonstrate the ability to reproduce these patterns in treatment. It would, however, be impossible to do so in all cases because of the reasons outlined previously.

The inclusion of intravaginal sources we believe to be highly desirable and will certainly help improve the prognoses of the cases treated by irradiation either exclusively or associated with surgery.

A recent review of the cases treated by irradiation at the Barnes and Barnard Hospitals in St. Louis over the past thirty years demonstrated a direct and constant correlation between prognoses and cancerocidal levels of irradiation at specified points on the outer surface of the uterus. Since the isodose curves, shown by Dr. Loeffler, which pass through Point A do not extend to the outer surfaces of the uterus and in some instances lie within the confines of the cavity itself, we hesitate to accept Point A as a reference point for corpus cancer as we do for cervical cancer. We feel that a point on the outer surface of the uterus, or the Point C, suggested by Costolow and Nolan, would be a more preferable critical point.

One other interesting feature we noted, and one which is important in selection of a critical dose, was the fact that the cancerocidal levels for endometrial cancer were 1,000 to 1,500 roentgens greater than for cervical cancer at the same intensity of exposure. The author, however, does not claim that his selected dose of 5,000 roentgens is the therapeutic goal but rather an experimental standard selected for the present.

We heartily agree with him in his statement that the system he outlines giving known dosages to definite points will be of positive value in a better understanding of the effects on tumor and adjacent normal tissue when related to results. A study such as this correlated with observed results will make it possible in the future to minimize both recurrences and complications which are due to presently unsuspected inadequate and excessive dosages.

Such studies which elevate radiotherapy from empiricisms and direct it toward a more rational and scientific approach will continue to improve the results of radiotherapy.

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THE RESULTS OF RADIATION THERAPY FOR RECURRENT CANCER OF THE CERVIX UTERI*

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THERE is apparently little uniformity of medical opinion regarding the efficacy of employing irradiation for the treatment of recurrent cancer of the cervix uteri. The usual clinical impression is that the primary treatment, whether radiologic or surgical, is the deciding factor in determining the outcome of this disease and that if the initial therapy is unsuccessful, supplemental irradiation will be at best only palliative in effect. A search of the literature reveals that there has been perhaps only a single review of cases in an effort to determine the results of irradiation in the retreatment of cervical carcinoma. This study was reported by Calkins in 1948, and is based on 500 consecutive cases in which cervical carcinoma was treated initially with irradiation. Supplemental irradiation was administered to 233 patients. One hundred and sixty of these patients received supplemental therapy because the disease had remained active following primary therapy, and of this group 28 patients survived for five years or longer. However, included in this group of survivors are 10 patients who were treated "on suspicion" only. The remaining 73 patients received additional therapy because a recurrence, either local or distant, developed following a completely satisfactory initial eradication of the primary lesion. Of this group of 73 patients who had recurrent carcinoma, 7 survived more than five years.

Because of the paucity of available information on this subject, we have reviewed the results of radiation therapy in the treatment of recurrent cancer of the cervix at the Mayo Clinic. Included are all cases in which definite recurrence was diagnosed and treated during the period 1940 to 1947, inclusive. The primary treatment may have been either irradiation, surgery, or a combination of irradiation and surgery. In many instances the primary treatment was not administered at the Mayo Clinic.

Initially, it was necessary to define, for the purpose of this study, those cases which would be included as recurrent cancer of the cervix. We decided that to be considered a recurrence, an interval of at least six months should have elapsed between completion of primary treatment and diagnosis of recurrent malignancy. Thus we were able to eliminate those cases with immediate recurrence, which usually indicates initial lack of response or only partial response to treatment. This initial poor response is frequently due to the far-advanced state of the disease. To include the lack of response of such far-advanced lesions (most of which were treated for palliation only) in the category of recurrence could serve no useful purpose in the evaluation of any form of treatment for recurrent cancer. However, following initial primary treatment, some lesions will have regressed only partially, and additional therapy (radiation or surgery) may be given in an effort to eradicate the disease completely. For purposes of this study such additional therapy is considered as part of the primary treatment if it was given within six months of completion of the initial treatment. Such a patient would later be considered as having a recurrence if a diagnosis of recurrent cancer were established more than six months subsequent to completing her intermittent course of primary treatment.

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† The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

TABLE I

DISTRIBUTION OF CASES BY INITIAL STAGE*

Stage	Number	Per Cent
I	4	3.6
II	32	29.1
III	43	39.1
IV	15	13.6
Not known	16	14.6
Total	110	100.0

* League of Nations' classification.

A total of approximately 1,200 cases of cancer of the cervix were reviewed. In 110 of these cases a recurrence developed which was diagnosed and treated with irradiation during the period 1940 to 1947, inclusive. It is this group of 110 cases with which we are concerned in this study.

The initial extent of disease in these cases according to the League of Nations' classification is given in Table I. Sixteen cases are not staged. All of these received their diagnosis and primary treatment elsewhere without the benefit of staging.

The primary treatment employed for the great majority of these patients was irradiation (Table II). Only 11 patients received surgery alone, and an additional 3 received surgery following irradiation. No patients were treated by means of external irradiation alone.

TABLE II

PRIMARY TREATMENT IN CASES IN WHICH CANCER LATER RECURRED

	Number	Per Cent
Irradiation only (total)	96	87.3
Radium and roentgen therapy	85	77.3
Radium only	10	9.1
Transvaginal and external roentgen therapy	1	0.9
Surgery only (total)	11	10.0
Total abdominal hysterectomy	8*	7.3
Wertheim hysterectomy	3	2.7
Irradiation followed by surgery	3	2.7
Total	110	100.0

* Five with bilateral salpingo-oophorectomy.

We have classified these patients according to age at the time of primary treatment (Table III) as a means of determining whether the mean age for cancer of the cervix as a whole differs markedly from the mean age for our patients in whom recurrence later developed. We found no statistically significant variation. Bowing,[1] who reviewed 2,246 patients with cancer of the cervix at the Mayo Clinic, found the mean age to be 49.1 years; the youngest patient was 21 years old, and the oldest 82. We found for our 110 patients in whom recurrence developed that the mean age was 47.3 years; the youngest patient was 27 years old, and the oldest 72. Similarly, we classified our patients in whom recurrence developed according to initial age and stage of the lesion. There was some indication of a relation of age to stage of disease, the cases with Stages I and II being younger on the average (45.8 years) than those of Stages III and IV (49.5 years), but again these average ages do not differ significantly from those previously reported by Bowing when he reviewed his series of patients with cancer of the cervix.

We have also compared the histopathologic diagnosis of our cases in which recurrence developed with those Bowing tabulated in his study of cancer of the cervix.

TABLE III

AGE AT TIME OF INITIAL TREATMENT

Age, Years	Number	Per Cent
20–29	3	2.7
30–39	35	31.9
40–49	23	20.9
50–59	33	30.0
60–69	14	12.7
70+	2	1.8
Total	110	100.0
Mean	47.3 years	
Youngest	27 years	
Oldest	72 years	

He found that 49.0 per cent of cases were squamous cell carcinoma, 31.8 per cent were adenocarcinoma, and 18.5 per cent were carcinoma, type not specified, and 0.7 per cent were epithelioma and adenocarcinoma. For our cases of recurrent carcinoma there was 90.9 per cent squamous cell carcinoma, 7.3 per cent adenocarcinoma and 1.8 per cent other. Even if most of Bowing's cases of "type not specified" were actually squamous cell, there would still be a much lower percentage of this type of lesion in his series than we found in our series of recurrent cases. Contrariwise, in our cases there is a much lower percentage of adenocarcinoma than Bowing found in his over-all study of cancer of the cervix.

It is well known that the majority of patients who develop a recurrence of cancer of the cervix will do so within the first two years following primary treatment. We were able to verify this when we analyzed our own cases. It will be seen (Table IV) that 80 per cent of recurrences occurred during the first two years, while only 3.6 per cent occurred after the fifth year.

When a recurrence has progressed sufficiently to produce symptoms or to permit diagnosis, it has in the majority of patients already spread to involve more than a single organ or structure (Table V). We found the cervix, vagina and parametrium to be involved in 43 per cent of cases, the cervix and vagina or vulva in about 4 per cent, the rectum or bladder along with involvement of other pelvic structures in about 7 per cent, and still other multiple areas of involvement in about 10 per cent.

TABLE IV

INTERVAL BETWEEN PRIMARY TREATMENT AND RECURRENCE

Interval, Months	Number	Per Cent
6–12	52	47.3
12–24	36	32.7
24–36	12	10.9
36–60	6	5.5
60+	4	3.6
Total	110	100.0

TABLE V

FIVE YEAR SURVIVAL RATE IN RELATION TO LOCATION OF RECURRENCE

Location	Number*	Lived 5 or More Years	
		Number	Survival rate, per cent
Cervix or uterus	5	3	60.0
Vagina	2	2	100.0
Cervix and vagina†	4	2	50.0
Cervix, vagina, parametrium	47	5	10.6
Parametrium	26	2	7.7
Other‡	26	4	15.4
Total	110	18	16.4

* Inquiry as of January 1, 1953.
† Includes 1 case with involvement of cervix and vulva.
‡ Includes cases with rectal, vesical, and urethral involvement; also distant and bony metastasis.

A primary histopathologic diagnosis was obtained for all of our patients except one. This patient received primary therapy elsewhere without benefit of histopathologic examination. She was examined at the clinic eleven months later because of an extensive recurrence which involved the vagina, uterus and parametrium, so that the pelvis was completely frozen. There was so much local necrosis that it was impossible to excise viable tissue for histopathologic examination without excessive risk of hemorrhage. This patient was given palliative radiation therapy; she lived only five months.

Positive histopathologic proof of recurrence was obtained for every patient in whom the recurrence was accessible with the exception of the single patient already described. There were 6 patients with pulmonary and 2 with bone metastasis for whom roentgenographic findings were accepted as evidence of recurrence. In addition, 26 patients had parametrial recurrence which was diagnosed on a basis of

TABLE VI

SURVIVAL RATES BY STAGE

Stage	Patients*	Lived 3 or More Years		Lived 5 or More Years	
		Number	Survival rate, per cent	Number	Survival rate, per cent
I	4	2	50.0	2	50.0
II	32	8	25.0	6	18.8
III	43	7	16.3	5	11.6
IV	15	3	20.0	2	13.3
Unknown	16	5	31.3	3	18.8
Total	110	25	22.7	18	16.4

* Inquiry as of January 1, 1953.

clinical findings only. However, each of these cases has been carefully evaluated and only those have been accepted for inclusion in this study who were examined by at least two physicians who agreed that a definite recurrence existed. Only 2 of these 26 patients survived more than five years. Several patients who were treated for "suspicion of parametrial recurrence" were not included in this study; interestingly, all of these survived more than five years.

All of our 110 patients who had recurrent cancer of the cervix received radiation therapy directed toward alleviation of the recurrence. Four patients received surgical treatment in addition to irradiation. Twenty-five patients (22.7 per cent) lived more than three years following treatment for the recurrence, and 18 patients (16.4 per cent) lived more than five years.

The relationship between survival rate and location of recurrence is given in Table v. As might be expected, there seems to be a better chance for control or eradication of the recurrence if it is localized within the "accessible" pelvic organs, that is, uterus, cervix, or vagina, than if it is localized elsewhere. Every patient in this category received radium therapy and nearly all received roentgen therapy also. The radium was employed in general according to the principles of the intensive broken-dose technique,[1] although, of course, it was necessary to individualize to a considerable extent. Two patients who have lived more than five years were treated successfully for vesicovaginal fistulas. Another patient was treated extensively with roentgen rays for metastasis to the lumbar vertebrae. She lived for eight years. A fourth patient was treated successfully with radium for a metastatic lesion of the buttock.

Operation was performed on 4 patients for recurrent carcinoma of the cervix. Two of these patients (both initially Stage III) have lived more than five years. One had recurrence in the cervix; a total abdominal hysterectomy and bilateral salpingo-oopho-

TABLE VII

FIVE YEAR SURVIVAL RATE, ACCORDING TO HISTOPATHOLOGIC DIAGNOSIS

Histopathologic Diagnosis	Patients*	Lived 5 or More Years	
		Number	Survival rate, per cent
Squamous cell epithelioma†	100	17	17.0
Adenocarcinoma	8	1	12.5
Other‡	2	0	0.0
Total	110	18	16.4

* Inquiry as of January 1, 1953.

† Of the 100 cases of squamous cell epithelioma, 8 were Grade 2, 54 Grade 3, 38 Grade 4. Of the 8 cases of adenocarcinoma, 3 were Grade 2, 4 were Grade 3, and 1 was Grade 4.

‡ One case hemangio-endothelioma, 1 case histopathologic diagnosis not known.

rectomy was performed which was followed by roentgen therapy. The other patient also had a recurrence in the cervix, and she too received a total abdominal hysterectomy and bilateral salpingo-oophorectomy followed by roentgen therapy. However, nearly three years later, a recurrence occurred in the vulva which was successfully treated with radium.

In Table VI the survival rates are expressed according to extent or stage of disease at the time the primary diagnosis was made. In general, the prognosis in the treatment of recurrence is poorer when the initial extent of the disease is more advanced than when it is less advanced.

Finally, we have given in Table VII the five year survival rate according to histopathologic diagnosis. Of the 18 patients who survived more than five years, 1 had a histopathologic diagnosis of Grade 2 squamous cell carcinoma, 11 cases were Grade 3, and 5 cases were Grade 4; only 1 survivor had adenocarcinoma and this was Grade 2.

SUMMARY AND CONCLUSIONS

This study has comprised a review of the results of radiation therapy in the treatment of 110 patients with recurrent cancer of the cervix at the Mayo Clinic during the period 1940–1947, inclusive. Four patients received surgical treatment in addition to irradiation. Of the entire group, 25 patients (22.7 per cent) lived more than three years following treatment for recurrence, and 18 patients (16.4 per cent) lived more than five years. This result is far from excellent, but it is sufficient to partially refute the impression that the prognosis is largely determined at the time of primary diagnosis and treatment. Furthermore, detailed study of the records of our patients who did not survive at least three years following treatment for recurrence reveals that in a great many cases worthwhile palliation was achieved.

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NATIONAL SURVEY OF CONGENITAL MALFORMATIONS RESULTING FROM EXPOSURE TO ROENTGEN RADIATION*

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SCOPE OF THE STUDY

IN OCTOBER, 1951, questionnaires (Fig. 1) were sent to 3,751 radiologists whose names were obtained from the directory of the American College of Radiology and from the rosters of each of the radiological societies in each state of the United States. Identical questionnaires were sent to 3,858 physicians in the medical specialties of anesthesiology, ophthalmology, pathology, plastic surgery and psychiatry and neurology.

The names of these physicians were obtained from the Directory of Medical Specialists, 1951 edition, and the mailing lists of the American College of Anesthesiology, Ophthalmology and Pathology respectively. Each questionnaire was accompanied by a letter soliciting cooperation in returning the schedule. Persons who did not respond within approximately two months were sent a second questionnaire together with a further appeal that it be returned.

RESPONSE TO THE SURVEY

Of the radiologists, 74.1 per cent returned the questionnaires, while 53.8 per cent of the controls responded.

Since women physicians constituted so small a portion of the returns and since the possible effects of radiation on the progeny of this group presents a different problem from that of radiation of the male, this paper, for the most part, will concern only male responders. Table 1 and Figure 2 show a breakdown of the returns according to sex.

There were 70 radiologists and 59 non-radiologists who returned questionnaires that were incompletely filled out and were not usable. Of these, 53 and 48 respectively were from persons who were married and reported offspring. Insofar as the available information indicates, these persons differ very little from those who fully completed the schedules. This group will not be included in any tables after the first six which deal with the "response to the survey."

Included among those recorded as "not returned" are 109 radiologists and 105 non-radiologists who were reported as dead or whose questionnaires were returned unclaimed.

Of the "controls" who returned questionnaires, the pathologists responded most readily (68.4 per cent) while the psychiatrists, anesthesiologists and plastic surgeons responded less readily in the order listed. Ophthalmologists responded least readily of all the groups, returning 43.6 per cent of the questionnaires mailed to them. Table II shows the breakdown of returns of controls according to specialty.

Figure 3 shows how the questionnaires were distributed throughout the United States. It also shows the percentage of radiologists and the percentage of non-radiologists who returned the questionnaires.

DECADE OF BIRTH

The year of birth of persons to whom questionnaires were sent was obtained from

* This investigation was supported by a research grant from the National Institutes of Health, United States Public Health Service.

Date _____

1. Your date of birth _____ Sex _____
   Marital status: Single _____ Married _____ Widowed or Divorced _____
2. Calendar years during which you have been regularly exposed to radiation, even though with protective equipment in the following fields (example: 1944-50; 1940-47):
   X-ray diagnosis other than fluoroscopy (positioning and exposing films) _____
   Fluoroscopy _____
   X-ray Therapy _____
   Radium Therapy _____
   Radioisotopes or other (explain) _____
   Never regularly exposed (check if applicable) _____
3. During any of these periods did you have inadequate protection or exposure greater than the accepted tolerance limits? Yes _____ No _____ If yes, during which years? _____
4. Was your father a worker in the field of radiation? Yes _____ No _____ If yes, was it prior to your birth? _____ At the time of your birth? _____ After your birth? _____
5. Was your mother a worker in the field of radiation? Yes _____ No _____ If yes, was it prior to your birth? _____ During gestation? _____ After your birth? _____
6. If you are or were married, what was the date of birth of your spouse? _____ (needed in analyzing data on comparative fertility)
7. If you are or were married give the inclusive period or periods of marriage (also needed for fertility studies. Give dates -- i.e., Oct. 1939 to Feb. 1948 or June 1946 to present) _____
8. If you are married, widowed, or divorced, did your spouse ever work in the field of radiation either before or after your marriage? Yes _____ No _____
9. If yes, during which calendar years? _____
10. Please list below all births, stillbirths, or miscarriages in your immediate family in order of occurrence of pregnancy:

Order No. 1, 2, 3 etc.	Date of Birth or Miscarriage	Sex	Normal, Congenital Defect, Miscarriage, or Stillborn (state below)	Type of Defect	Time of Miscarriage (month of gestation)

11. Have any of these children developed defects during childhood, though apparently born normal? If so, which child (above order number)? _____
    At what age? _____ Type of defect _____
12. Did the mother have rubella or any other virus infection during any of the above pregnancies? Yes _____ No _____ If yes, pregnancy number _____ Type of infection _____
13. Did the mother have any auto accidents or other trauma? Yes _____ No _____
    If yes, pregnancy number _____
14. Are there any anomalies in the family of either yourself or your spouse (you, your spouse, a father, a mother, brother, sister, brothers, or sisters children, etc.) Yes _____ No _____ If yes, explain relationship and type of defect _____
15. Do you know of any workers in radiation whose offspring show congenital abnormalities? (If so, please elaborate on type of defect) _____
16. Do you know of any cases of abortions, anomalies, or both, resulting from accidental or therapeutic radiation during pregnancy? If so, give description of defect and if possible details concerning radiation the patient received. _____
17. Please make any observations or comments which may be helpful in this study.

Thank you for your cooperation. No signature required.

WCH Form

FIG. 1. The questionnaire.

directories of the medical specialties and from the questionnaires. Table III reveals that the male radiologists were, as a group, slightly older than the male nonradiologists. Persons born prior to 1895 constituted 20.8 per cent of the radiologists and

TABLE I

RESPONSE TO SURVEY

	Males				Females			
	Radiologists		Nonradiologists		Radiologists		Nonradiologists	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Returned	2,717	74.3	1,918	53.5	62	66.7	156	57.6
Not returned	941	25.7	1,669	46.5	31	33.3	115	42.4
Total sent	3,658	100.0	3,587	100.0	93	100.0	271	100.0

17.3 per cent of the nonradiologists. Although the response of nonradiologists was less than that of radiologists at each age, the poorer response of nonradiologists was more marked in the older age groups, as may be seen in Table IV and Figure 4.

DEFINITIONS

In this presentation "married" means the responders are or were once married and "single" means they were never married. The term "offspring" means a product of conception whether aborted, stillborn, defective or normal.

When the term "exposed" is used in this report, it means those respondents were then engaged or had been working in a field where equipment which gives off ionizing radiation was used. The actual extent to which these persons received such radiation is unknown, varying with the type of equipment used, procedures employed, volume of practice, and other detailed factors which could not be quantitatively assessed in this survey. It was further seen from the individual questionnaires there were sometimes "breaks" in the periods of exposure. There were also a number of cases where persons left radiation work prior to the end of the usual

TABLE II

RESPONSE OF NONRADIOLOGISTS ACCORDING TO MEDICAL SPECIALTY

Specialty	Sent	Returned	Per Cent Returned
Anesthesiologists	602	331	55.0
Ophthalmologists	1,451	633	43.6
Pathologists	838	573	68.4
Plastic surgeons	197	103	52.3
Psychiatrists and neurologists	770	434	56.4
Total	3,858	2,074	53.8

More radiologists returned forms than nonradiologists, and more men than women responded to the questionaires.

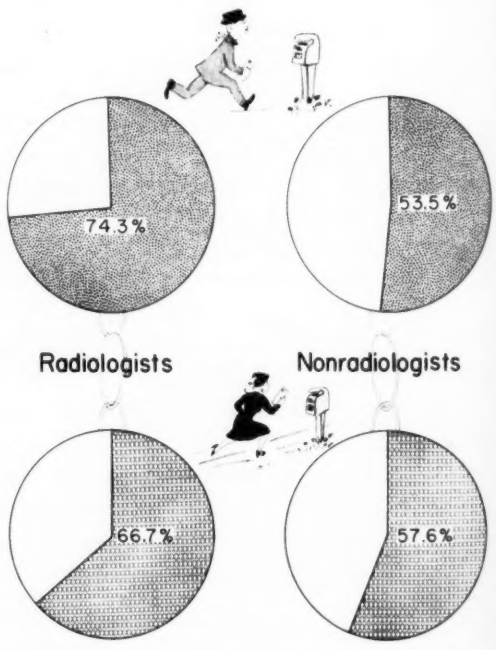

FIG. 2. Chart demonstrating that more male radiologists than male controls and more female radiologists than female controls returned the questionnaires.

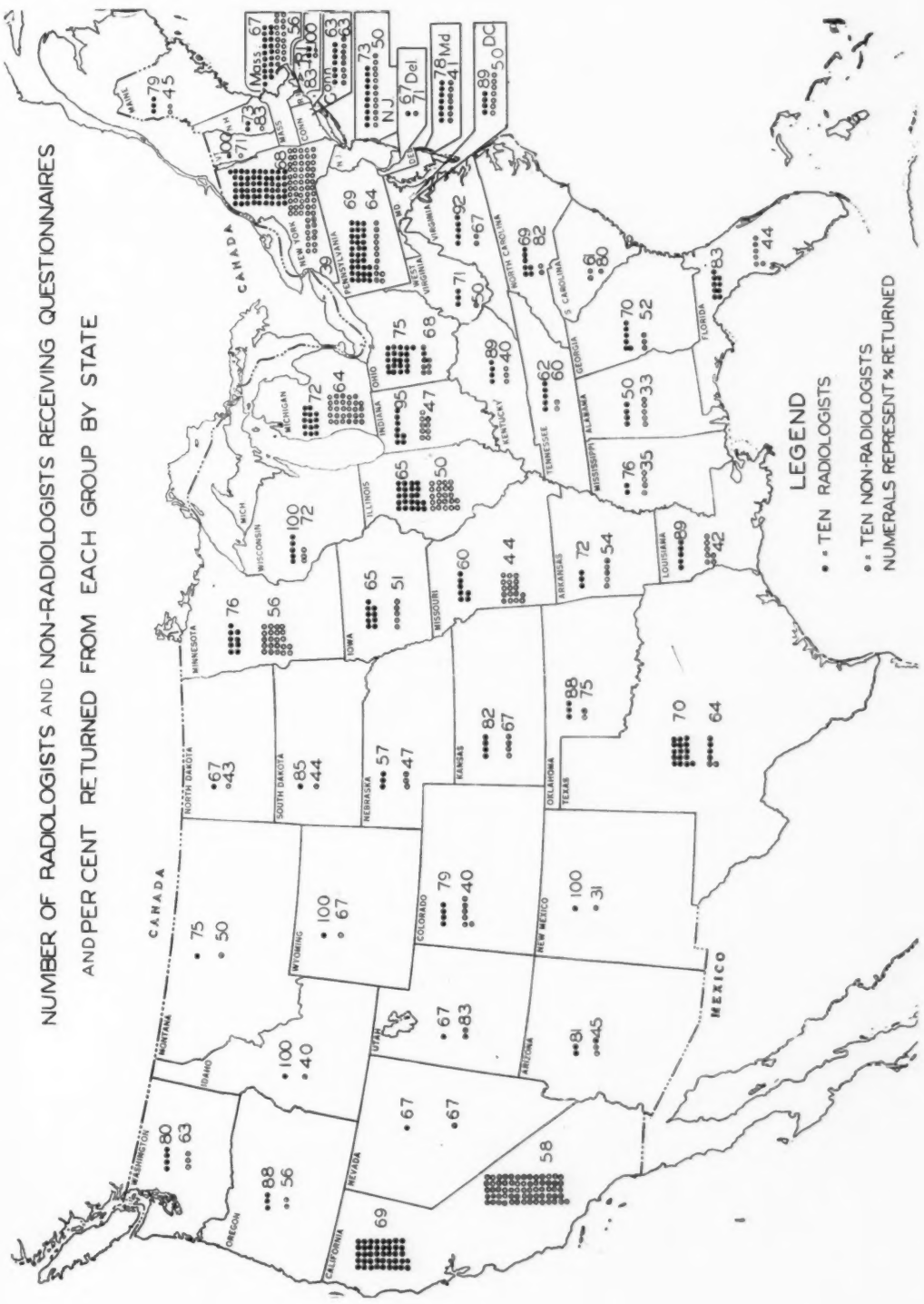
NUMBER OF RADIOLOGISTS AND NON-RADIOLOGISTS RECEIVING QUESTIONNAIRES
AND PER CENT RETURNED FROM EACH GROUP BY STATE
LEGEND
• - TEN RADIOLOGISTS
•: TEN NON-RADIOLOGISTS
NUMERALS REPRESENT % RETURNED
CANADA
MEXICO
WASHINGTON
OREGON
CALIFORNIA
IDAHO
NEVADA
MONTANA
WYOMING
UTAH
ARIZONA
COLORADO
NEW MEXICO
NORTH DAKOTA
SOUTH DAKOTA
NEBRASKA
KANSAS
OKLAHOMA
TEXAS
MINNESOTA
IOWA
MISSOURI
ARKANSAS
LOUISIANA
WISCONSIN
ILLINOIS
MICHIGAN
INDIANA
OHIO
KENTUCKY
TENNESSEE
MISSISSIPPI
ALABAMA
GEORGIA
FLORIDA
S. CAROLINA
NORTH CAROLINA
VIRGINIA
WEST VIRGINIA
PENNSYLVANIA
NEW YORK
MAINE
VT.
N.H.
MASS.
R.I.
CONN.
N.J.
DEL.
MD.
D.C.

FIG. 3.

TABLE III

AGE DISTRIBUTION OF MALES

Year of Birth	Radiologists						Nonradiologists					
	Not returned		Returned		Total sent		Not returned		Returned		Total sent	
1915+	132	14.0	712	26.2	844	23.1	219	13.1	564	29.4	783	21.8
1905–1914	252	26.8	1,043	38.4	1,295	35.4	590	35.4	812	42.3	1,402	39.1
1895–1904	212	22.5	494	18.2	706	19.3	433	25.9	328	17.1	761	21.2
1885–1894	191	20.3	315	11.6	506	13.8	247	14.8	138	7.2	385	10.7
–1884	125	13.3	133	4.9	258	7.1	168	10.1	69	3.6	237	6.6
Unknown	29	3.1	20	0.7	49	1.3	12	0.7	7	0.4	19	0.5
All	941	100.0	2,717	100.0	3,658	100.0	1,669	100.0	1,918	100.0	3,587	99.9

reproductive span of the marital union. In some cases lack of precision in recording dates would have further complicated any attempt to compute just when births occurred relative to "breaks" in radiation experience. For this reason, it was decided to classify with the exposed group all births occurring either during or after exposure of the father. A further reason for this decision was that genetic damage that may have occurred as a result of exposure might affect all offspring subsequent to the

TABLE IV

RESPONSE TO SURVEY ACCORDING TO AGE

MALE RADIOLOGISTS

Year of Birth	First Letter			Second Letter			Both Letters		
	Sent	Ret.	% Ret.	Sent	Ret.	% Ret.	Sent	Ret.	% Ret.
1915+	844	560	66.35	284	152	53.52	844	712	84.36
1905–1914	1,295	820	63.32	475	223	46.95	1,295	1,043	80.54
1895–1904	706	374	52.97	332	120	36.14	706	494	69.97
1885–1894	506	242	47.83	264	73	27.65	506	315	62.25
–1884	258	90	34.84	168	43	25.60	258	133	51.55
Unknown	49	9	18.37	40	11	27.50	49	20	40.82
All radiologists	3,658	2,095	57.27	1,563	622	39.80	3,658	2,717	74.28

MALE CONTROLS—NONRADIOLOGISTS

Year of Birth	First Letter			Second Letter			Both Letters		
	Sent	Ret.	% Ret.	Sent	Ret.	% Ret.	Sent	Ret.	% Ret.
1915+	783	391	49.94	392	173	44.13	783	564	72.03
1905–1914	1,402	532	37.95	870	280	32.18	1,402	812	57.92
1895–1904	761	175	23.00	586	153	26.11	761	328	43.10
1885–1894	385	78	20.26	307	60	19.54	385	138	35.84
–1884	237	40	16.88	197	29	14.72	237	69	29.11
Unknown	19	1	5.26	18	6	33.33	19	7	36.84
All controls	3,587	1,217	33.93	2,370	701	29.58	3,587	1,918	53.47

exposure and not just those conceived while the father was engaged in radiation work.

The variations from normal considered in this report have been broadly grouped as multiple births, fetal deaths, and congenital defects. These are defined as follows:

Multiple Births. In the returns from this survey there were no multiple births higher than twins. In the tables that follow, if a twin was also a fetal death or congenital defective it was also included with the abnormality which applied. Where the term "normal" is used the figures include twins which were normal in all respects except twinning.

Fetal Death. Fetal death includes all reported cases where the product of conception was not born alive. It therefore includes miscarriages and still births irrespective of the length of uterogestation and regardless of whether or not the embryo or fetus was otherwise normal at this stage.

Congenital Defective. Included as congenital defectives are defects listed as congenital malformation in the "Manual of International Statistical Classification of Diseases, Injuries and Causes of Death," 1948. The principal classifications included are congenital malformations of various systems, 750 through 759; muscular defects reported as congenital under 745 through 749; congenital anomalies of the teeth under 533.5; defects of the eyes reported as congenital under 380–389; congenital deafness under 398; mental deficiency under 325; and neoplasms reported as congenital, under 220 and 228.

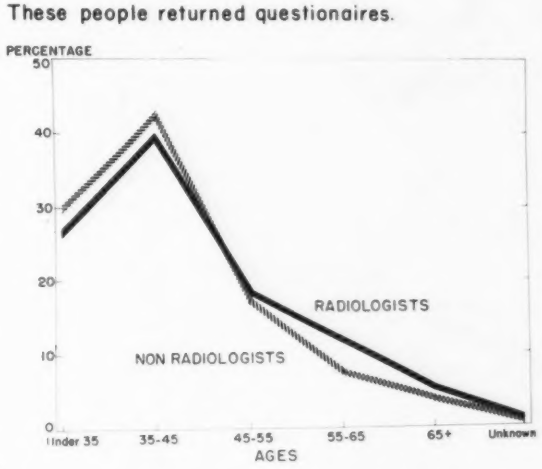

FIG. 4. Age distribution of radiologists and of nonradiologists who returned questionnaires.

Other defects reported as congenital fall under a number of other classifications in the Manual. Not included among the defects in this report are spastics (340), birth injuries (760 and 761) or the product of placental abnormalities (640 through 649).

BIAS

In any survey possible bias due to differences in interest must be considered, even where the groups are presumed to be

TABLE V

RESPONSE BY MARITAL AND REPRODUCTIVE STATUS

	Radiologists							Nonradiologists						
	1st letter		2nd letter		Both letters		Per cent response to 1st letter	1st letter		2nd letter		Both letters		Per cent response to 1st letter
	No.	Per cent	No.	Per cent	No.	Per cent		No.	Per cent	No.	Per cent	No.	Per cent	
Married, offspring	1,755	83.9	481	77.3	2,236	82.4	78.5	1,002	82.7	568	81.0	1,570	82.1	63.8
Married, No. offspring	266	12.7	106	17.0	372	13.7	71.5	157	13.0	95	13.6	252	13.2	62.3
Single	71	3.4	35	5.6	106	3.9	67.0	53	4.4	38	5.4	91	4.8	58.2
All	2,092	100.0	622	99.9	2,714*	100.0	77.1	1,212	100.1	701	100.0	1,913†	100.1	63.3

* Does not include 3 persons of unknown status.
† Does not include 5 persons of unknown status.

TABLE VI

OFFSPRING PER RESPONDENT—MALES, MARRIED, WITH OFFSPRING

	First Response			Second Response			Total Response		
	No. of persons	No. of offspring	Offspring per person	No. of persons	No. of offspring	Offspring per person	No. of persons	No. of offspring	Offspring per person
Radiologists	1,755	4,717	2.69	481	1,290	2.68	2,236	6,007	2.69
Nonradiologists	1,002	2,658	2.65	568	1,541	2.71	1,570	4,199	2.67

homogeneous with respect to education and economic level. Responses to the first and second questionnaires indicate the extent of the problem in this study, even though information on the nonresponders is not available. Table V shows the responses according to marital and reproductive status.

It will be noted that within the groups of both radiologists and nonradiologists, persons with offspring responded most readily, married persons without offspring somewhat slower, and single persons least readily. Difference in this respect is more evident in the radiologists than in nonradiologists. However, the over-all proportion of response by marital and reproductive status shows no statistically significant differences between the two groups.

Table VI gives the number of offspring of radiologists and nonradiologists who had produced offspring. By this crude measure, the small differences between the two groups and between first and second responses within each group gave no indication of interest bias due to size of family. Fertility of exposed and unexposed persons is discussed in detail in a later section of this paper. No conclusions concerning their fertility should be attempted from Table VI.

All of the radiologists who replied to this survey had worked with radiation producing equipment. Among the 1,918 nonradiologists, it was found that 371 had also employed such equipment in their work and were therefore exposed to radiation hazards. Responses of exposed and unexposed nonradiologists are shown in Table VII. Greater interest in the survey on the part of nonradiologists with radiation experience probably explains their higher response to the first questionnaire.

In summary, the response of nonradiologists was considerably poorer than that of radiologists. Consistent with this is the apparently higher response of nonradiologists who had radiation experience compared to nonradiologists without radiation experience, as judged from replies to the first and second questionnaires. Radiologists surveyed were slightly older, as a

TABLE VII

RESPONSE OF NONRADIOLOGISTS EXPOSED AND NOT EXPOSED TO RADIATION

	1st Letter		2nd Letter		Both Letters		Per Cent response to 1st letter
	No.	Per cent	No.	Per cent	No.	Per cent	
Exposed	250	20.63	121	17.26	371	19.39	67.37
Not exposed	962	79.37	580	82.74	1,542	80.61	62.39
All	1,212	100.00	701	100.00	1,913	100.00	63.36

group, than the nonradiologists. In proportion to the returns from all ages, the older radiologists responded better than the older nonradiologists.

Responding radiologists and nonradiologists are very nearly the same in proportions of married persons, persons with offspring, and single persons. For persons who have had offspring, there are approximately the same number of offspring per person among the radiologists as among nonradiologists. In these respects there is probably little bias between groups, although the waves of response shown in Table v would indicate that both groups are underrepresented in single persons and in persons without offspring. Single and childless respondents replied to the second appeal in higher proportion than to the first letter. Possible bias with respect to reporting of abnormalities among offspring will be discussed in a subsequent section.

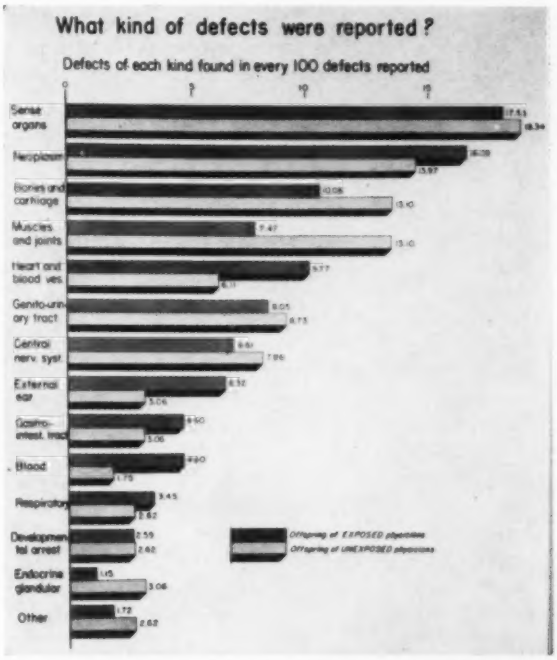

FIG. 5. Chart showing kinds and per cent of defects reported by exposed and unexposed physicians.

VARIATIONS FROM NORMAL

Multiple births, fetal deaths, and congenital defectives, as defined above were considered as variations from normal.

Table VIII and Figure 5 show, by broad groups, the defects reported, together with the proportional distribution of these defects among the defective offspring of exposed and unexposed persons. The "exposed" column includes defective offspring who were born during or after radiation experience of the father, while the "unexposed" column includes defective offspring born prior to radiation experience of the father and to fathers who had no radiation experience. In this table there are more defects shown than there were defective offspring reported, due to multiple defects in some offspring. Multiple defects are included, however, only where they are essentially different defects. For example, in Tables VIII and IX (and in these tables only) two defects are recorded for the child who had a harelip and a ventricular septal defect, but only one defect is recorded for the child with harelip and cleft palate.

Taken together, the proportional distribution of defects of the exposed shows no statistically significant difference* from that of the unexposed. This is what one would expect from the results of experimentation on lower animals, where radiation does not produce new kinds of anomalies nor change the proportions of the various kinds of defects that occur in nonradiated populations. However, when the defects of Tables VIII and IX are examined in detail it is seen that exposed persons reported a significantly higher proportion of heart and blood vessel and blood anomalies when these are totaled together, while unexposed persons reported a significantly higher proportion of muscle and joint defects. These differences are difficult to explain even on the basis of differential interests of the several medical specialists included in the survey. Differences by medical specialty will be examined in a future report.

* Except where otherwise noted, statistical significance in this paper is based upon a chi-square test of independence, and the level of significance employed is 0.05.

TABLE VIII

DEFECTS AMONG OFFSPRING BY EXPOSED AND UNEXPOSED PERSONS

Type of Defect	International Classification of Diseases (1948) Code Number	Exposed		Unexposed	
		No.	Proportion	No.	Proportion
Heart and blood vessels	754.1, 754.2, 754.3, 754.4	34	9.77	14	6.11
Blood	770.0, 771.0	16	4.60	4	1.75
Respiratory tract	762, 759.0, 773.5	12	3.45	6	2.62
Muscles and joints	560.0, 560.2, 560.5, 561.0, 738, 744.1, 759.2	26	7.47	30	13.10
Bones and cartilage	733, 751, 758.0, 758.1, 758.2, 758.3, 758.4, 758.6, 746, 748, 759.1, 759.3	35	10.06	30	13.10
Gastrointestinal tract	756.0, 756.2, 545, 784.4	16	4.60	7	3.06
Genitourinary tract	757.0, 757.3, 759.3	28	8.05	20	8.73
Neoplasms	192, 200, 216, 220, 221, 223, 225, 226, 228, 289.0	56	16.09	32	13.97
External ear	759.3	22	6.32	7	3.06
Central nervous system	325.4, 325.5, 353, 367, 783, 753.1, 759.3	23	6.61	18	7.86
Sense organs	380, 384, 388, 398, 753.0, 753.1	61	17.53	42	18.34
Endocrine organs, other glandular	253, 260, 272, 273, 756.2, 587.2, 289.2	4	1.15	7	3.06
Developmental arrest	755, 759.3	9	2.59	6	2.62
Other	759.3, 713, 716, 533.7	6	1.72	6	2.62
All		348	100.01	229	100.00

CLASSIFICATION OF EXPOSED AND UNEXPOSED PERSONS

It was found that among the radiologists who were married and had offspring 981 had been working in radiology since before they were married. In this group, therefore, all of the offspring were born after the father had been exposed to radiation. There were 1,202 radiologists who entered this field at varying lengths of time after they were married. The children of these men were, in some cases, born prior to and, in some cases, born after the fathers were exposed to radiation. Similarly among the nonradiologists there were persons who were never exposed in radiation work, persons who were exposed since before they were married, and persons who entered radiation after they were married. Again in the last group in some cases the offspring were born prior to and in some cases after exposure of the father. Table X gives the number of persons and offspring in these several groups.

In the tables which follow, offspring born during or after exposure of the father will be compared with offspring born prior to exposure of the father. For this purpose Groups I and III of Table X will be combined into one class called "exposed throughout marriage." The offspring born during and after exposure from Groups II and IV will be combined into a single class called "exposed part of marriage." Offspring from Groups II and IV, born prior to exposure, will be combined into one class called "unexposed part of marriage." The last group will be the same as Group V of Table X and will be called "unexposed throughout marriage."

ABNORMALITIES REPORTED ON FIRST AND SECOND RESPONSES

The proportions of abnormal offspring reported in response to the first and second mailings by the several groups of exposed and unexposed are presented in Table XI. Abnormal offspring here includes fetal

Table IX

ALL DEFECTIVES

Terminology quoted from questionnaires

Anomalies	All Exposed	All Unexposed	Total
OF HEART AND BLOOD VESSELS			
Congenital heart defect	10	8	18
Congenital heart patent ductus (one with microphthalmia, cataract and hearing defect)	0	2	2
Congenital heart lesion (also had aplasia ear and cleft palate)	1	0	1
Cardiac left to right shunt	1	0	1
Heart defect	8	0	8
Cardiac anomaly (also had osteochondroma and lung lobe agenesis and lumbar spina bifida)	1	0	1
Mitral lesion	0	1	1
Patent foramen ovale	1	0	1
Patent interventricular septal defects (some of the exposed also had hemangioma, obstruction of right nasolacrimal duct and hydrocele)	5	1	6
Tetralogy of fallot	1	2	3
Cardiac (odontoma?)	1	0	1
Patent interatrial septum (narrow esophagus)	1	0	1
Tricuspid atresia	1	0	1
Patent ductus arteriosus	1	0	1
Congenital lymphedema both feet	1	0	1
Congenital occlusion splenic and umbilical vein	1	0	1
All heart and blood vessels	34	14	48
OF BLOOD			
Hemorrhagic disease	0	1	1
Erythroblastosis	14	3	17
Died 4 days RH positive problems	1	0	1
Vascular abnormal leg	1	0	1
All blood vessels	16	4	20
OF LUNGS AND RESPIRATORY			
Atelectasis (two of exposed also had atresia of esophagus)	7	3	10
Congenital atelectasis (and agenesis of kidneys)	2	0	2
Undeveloped lung	3	0	3
Cyanosis (immature)	0	1	1
Laryngeal stenosis	0	2	2
All lung and respiratory defects	12	6	18
OF MUSCLES AND JOINTS			
Absence of diaphragm	1	2	3
Hernia (unexposed also had undescended testes)	2	2	4
Inguinal hernia (two of exposed also had strabismus and hydrocele)	11	6	17
Strangulated inguinal hernia	0	1	1
Diaphragmatic hernia	1	0	1
Umbilical hernia	0	6	6
Hydrocele hernia	0	1	1
Scrotal hernia	1	0	1
Hernia left indirect (cartilage spur on right ear)	1	0	1
Right hernia—male twins	0	2	2
Amyotonia congenita	0	1	1
Club feet	5	6	11
Muscular dystrophy	0	1	1
Oppenheim's disease	3	0	3
Congenital torticollis	1	0	1
Loose joints	0	1	1
Congenital defect diaphragm and ribs	0	1	1
All muscles and joints	26	30	56
OF BONES AND CARTILAGE			
Web toes (not designated familial)	0	2	2
Pes planus (one unexposed also had inversion of right foot)	2	4	6
Metatarsus varus	7	2	9
Foot rotation	1	1	2
Congenital anterior bowing (and atrophic testicles)	0	1	1
Talipes equino varus	1	0	1
Distal phalanx deformity (and one toe)	1	0	1
Deformed hands (one exposed also had a lesion of feet and heart)	2	5	7
Deformed feet	1	4	5
Defect knee—absent patella	1	0	1
Bilateral hip dysplasia	1	0	1
Deformed hip	1	0	1
Bilateral calcaneus valgus	1	0	1
Dislocated hip	0	3	3
Cervical vertebrae (6)	0	1	1
Congenital fragilitas ossium	0	1	1
Spondylolisthesis	1	0	1
Congenital hypoplasia acetabulum	1	0	1
Absence head of femur, fibula, short tibia	1	0	1
Congenital error in segment of dorsal spine	1	0	1
Skull defect	1	0	1
Minor syndachtylism toes	1	0	1
Deformity thoracic cage	1	0	1
Bone cyst fibula (spontaneous regression)	1	0	1
Spina bifida (one unexposed also had polydactylism, club foot, hemangiomas, ribs and diaphragm)	6	5	11
High palate (and prominent upper teeth)	1	0	1
Congenital malformed pelvis	0	1	1
Polydactylism	1	0	1
All bones and cartilage	35	30	65
OF GASTROINTESTINAL TRACT			
Atresia of intestine	0	1	1
Pyloric stenosis	9	1	10
Obstruction of duodenum	1	1	2
Congenital dysphagia	0	1	1
Esophageal stricture	1	2	3
Hyperplasia of colon	0	1	1
Celiac syndrome	2	0	2
Absence of abdominal wall	1	0	1
Gastrohepatic ligament	1	0	1
Atresia of esophagus	1	0	1
All gastrointestinal tract defects	16	7	23
OF GENITOURINARY TRACT			
Deformed kidney and/or ureter	1	0	1
Redundant mucosal folds of ureters	1	0	1
Congenital defect urachus	1	0	1

Table IX—(*continued*)

TABLE IX—(*continued*)

Anomalies	All Exposed	All Unexposed	Total
Right cryptorchism (testes undescended)	1	0	1
Extrophia	0	2	2
Infantile uterus	1	0	1
Glans hypospadius	4	5	9
Aplasia one kidney	0	1	1
Undescended testes	5	8	13
Hydronephrosis	0	1	1
Hydrocele	6	2	8
Atresia ureters	1	0	1
Duplicate kidneys and/or ureters	4	0	4
Obstruction left ureteropelvic junction hydronephrosis; aberrant artery	2	0	2
Agenesis of kidneys	1	0	1
Atrophic testicles	0	1	1
All genitourinary tract defects	28	20	48
NEOPLASMS			
Melanoma	1	1	2
Lymphosarcoma	1	0	1
Cutaneous xanthomatosis	1	0	1
Bony exostosis	0	1	1
Retinoblastoma	0	1	1
Lipoma (pilonidal cyst)	0	1	1
Dermoid cyst	0	1	1
Blush mark	3	0	3
Nevus—spider nevus	4	0	4
Pilonidal dimple	0	1	1
Pilonidal cyst (and/or pilonidal sinus)	2	4	6
Cystic hygroma	1	0	1
Angioma	2	0	2
Hemangioma (myopia, absence of lower incisor, congenital cataracts, eye, and pectus excavatum)	32	20	52
Lymphangioma	1	0	1
Osteochondroma	2	0	2
Multiple osteochondroma of lungs	1	0	1
Dermoid inclusion right eye	1	0	1
Diffuse hemangioma (and hemiatrophy)	1	0	1
Congenital cyst cervical cord	0	1	1
Pigmented nevus	1	0	1
Multiple black flat moles	1	0	1
Dermoid tragus (successfully removed)	1	0	1
Hairy nevus	0	1	1
Eosinophilic granuloma	1	0	1
All neoplasms	57	32	89
OF EXTERNAL EAR			
Defect outer ear	2	0	2
Absence tip or lobe	1	1	2
Accessory lobe	1	1	2
Notch in lobe	1	0	1
Accessory external ear	2	0	2
Bilateral fold in external ear canal	1	0	1
Anterior folding of ears	1	0	1
Extra auricular polyps	0	1	1
Unilateral microtia (and unilateral deafness)	2	0	2
Notch in helix left ear (and minimal webbing hands)	1	0	1
Defect ear	0	2	2
Small papule—anterior left ear—redupl. tragus	2	0	2
Slight underdeveloped right ear	1	0	1
Aplasia, ear	1	0	1
Accessory cartilage ear	2	1	3
Deformed left auricle	1	0	1

TABLE IX—(*continued*)

Anomalies	All Exposed	All Unexposed	Total
Right microtia	1	0	1
Defect tragus and antetragus	1	0	1
Small bump, left ear	1	0	1
Sebaceous cyst of ear	0	1	1
All external ear defects	0	1	1
All external ear defects	22	7	29
OF CENTRAL NERVOUS SYSTEM			
Tay-Sachs disease (idiocy)	0	1	1
Congenital malformed ears, pelvis and central nervous system	0	1	1
Mentally deficient (and convulsions)	2	2	4
Mongolism	3	3	6
Anencephaly	3	1	4
Hydrocephalus	1	4	5
Mental retardation (eosinophilic granuloma and epilepsy)	3	1	4
Porencephalic cyst	1	0	1
Convulsive seizures (petit mal or epilepsy)	3	0	3
Meningocele, anterior	1	0	1
Brain damage—craniostenosis	0	3	3
Cerebral aplasia	0	1	1
Cerebral dysgenesis	1	0	1
Cerebral hypoplasia	1	0	1
Encephalitis	3	1	4
6th, 7th, 8th cranial nerve paralysis	1	0	1
All central nervous system defects	23	18	41
OF SENSE ORGANS			
Coloboma (and encephalitis)	1	1	2
Congenital cataracts	3	1	4
"Epicanthus"	0	1	1
Ptosis of eyelid	2	1	3
Congenital eye defect	1	0	1
Malformed right eye (congenital blindness)	1	0	1
Defective night vision	2	0	2
Congenital iseikonia, left eye	1	0	1
Strabismus (hydrocele, pilonidal cyst, encephalitis)	16	14	30
Astigmatism	1	0	1
Paralysis right rectus	1	0	1
Retrolental fibrosis and microphthalmus	1	0	1
Congenital impaired optical fusion	1	0	1
Paralysis superior rectus muscle	0	1	1
Weakness rectus muscle	0	1	1
Congenital amblyopia	0	1	1
Hyperphoria (and one tooth upside down)	0	2	2
Squint	3	1	4
Myopia	15	13	28
Hyperopia	0	1	1
Congenital defect—lacrymal duct	3	0	3
Overconvergence—one eye (slight)	1	0	1
Congenital cataract and microphthalmus	0	1	1
Hearing defect	7	1	8
Congenital deafness	0	2	2
Unilateral deafness	1	0	1
All sense organ defects	61	42	103
OF ENDOCRINE ORGANS (OTHER GLANDULAR)			
Diabetes	1	0	1
Persistent thymus	1	0	1

TABLE IX—(*continued*)

Anomalies	All Exposed	All Unexposed	Total
Adrenal apoplexy	0	1	1
Pituitary dwarfism	0	1	1
Sudden death—thymic type	1	0	1
Hypogonadism—Froelich's	1	0	1
Pancreatic deficiency	0	1	1
Cystic fibrosis of pancreas	0	1	1
Enlarged thymus	0	1	1
Alkaptonuria	0	1	1
Creatinism	0	1	1
All endocrine defects	4	7	11
OF DEVELOPMENTAL ARREST			
Hare lip (and cleft palate)	3	0	3
Cleft palate	1	2	3
Cleft lip	0	2	2
Soft palate cleft	1	0	1
Soft palate irregularity	1	0	1
Accessory nipples	0	2	2
Thyroglossal cyst	1	0	1
Branchial cleft sinus	1	0	1
Unclosed neck, cleft, side	1	0	1
All developmental arrest	9	6	15
OTHER DEFECTS			
Congenital multiple defects	0	1	1
"Deformed"	2	0	2
Absence of hair follicles	1	0	1
Pigment disturbance area	1	3	4
Incisor teeth missing	0	1	1
Minus canine teeth	1	0	1
2 upper cuspids missing	0	1	1
Hemiatrophy (hemangioma)	1	0	1
All other defects	6	6	12
ALL DEFECTS	348	229	577

deaths and defects, but does not include twins who were otherwise normal. The assumption to be made from this table is that if a higher rate of abnormal offspring is reported in response to the second appeal than to the first, there is probably some nonresponse bias which results in underrepresentation of abnormalities in the respondent population. However, if the first responses show the higher rate of abnormalities, the bias is probably in the direction of an excess of defects among the offspring of respondents of such groups. Physicians who were exposed throughout their marriage and physicians who were unexposed throughout their marriage show the same trend of response—a trend which indicates that the rates of defects among offspring of these groups are probably lower than those of the populations from which these persons were the responders. For the group that was unexposed throughout marriage, the difference in rates of abnormality between the first and second response is significant at the 5 per cent level. For the group that was exposed throughout marriage, the difference is not statistically significant (P equals 0.15). Table XI indicates that for those groups that were exposed during part of their marriage there was possibly a bias toward answering the questionnaire when defects occurred during the exposed portion of marriage, although the differences in abnormality rates between responses are not statistically significant. It should be noted that these groups had the opportunity to compare children born after exposure with children born prior to exposure, whereas persons who were either exposed or unexposed throughout marriage did not have this opportunity.

It will be seen in subsequent tables that persons who were exposed and persons who were unexposed throughout marriage have similar distributions with respect to parity of offspring, date of birth of offspring, and ages of the mother at the time the offspring were born. It is recognized that while these two groups appear to be fairly homogeneous and while the response trends already described in conjunction with Table XI are in the same direction for these groups, this is not complete assurance that no bias differences exist. Since there is nonresponse, one cannot be certain how the nonresponders would have affected the rates either toward increasing or decreasing observed differences. But on the basis of observations among responders, comparisons between offspring of persons exposed throughout marriage and persons unexposed throughout marriage present the least possibility of bias.

RELATION OF PARITY ORDER TO ABNORMALITIES

Rates of normal offspring and variations from normal are given in Table XII for the

TABLE X

NUMBER OF OFFSPRING ACCORDING TO RADIATION WORK OF THE FATHER

Males with Offspring	No. of Persons	Number of Offspring		
		Prior to exposure	During and after exposure	All
I. Radiologists Exposed throughout reproductive span	981	—	2,522	2,522
II. Radiologists Exposed during part of reproductive span	1,202	1,087	2,266	3,353
III. Nonradiologists Exposed throughout reproductive span	134	—	366	366
IV. Nonradiologists Exposed during part of reproductive span	172	188	307	495
V. Nonradiologists never exposed	1,216	3,209	—	3,209
All	3,705	4,484	5,461	9,945

TABLE XI

PREVALENCE OF ABNORMAL OFFSPRING (FETAL DEATH AND CONGENITAL DEFECTS) AMONG SEVERAL GROUPS OF EXPOSED AND UNEXPOSED PERSONS IN RELATION TO RESPONSE TO FIRST AND SECOND QUESTIONNAIRES

Group	First Response				Second Response			
	Total offspring	Abnormal offspring	Per cent abnormal	Per cent abnormal adjusted for parity*	Total offspring	Abnormal offspring	Per cent abnormal	Per cent abnormal adjusted for parity*
Exposed throughout marriage	2,242	418	18.64	18.83	646	137	21.21	21.25
Exposed part of marriage	1,995	405	20.30	19.72	578	108	18.69	18.07
Unexposed part of marriage	951	136	14.30	15.36	324	50	15.43	16.16
Unexposed throughout marriage	2,026	334	16.49	16.51	1,183	233	19.70	19.70
All exposed	4,237	823	19.42	19.26	1,224	245	20.02	19.72
All unexposed	2,977	470	15.79	16.16	1,507	283	18.78	18.96
Total	7,214	1,293	17.92	17.92	2,731	528	19.33	19.33

* Adjusted for differences in parity using the parity distribution of all responders as the standard.

TABLE XII

PREVALENCE OF TWINS, FETAL DEATHS, CONGENITAL DEFECTS AND NORMAL OFFSPRING OF EXPOSED AND UNEXPOSED PERSONS ACCORDING TO ORDER OF BIRTH

Birth Order	Offspring of Persons:	Total Offspring	Twins		Fetal Deaths		Congenital Defects		Normal	
			No.	Per cent of total offspring	No.	Per cent of total offspring	No.	Per cent of total offspring	No.	Per cent of total offspring
1	Exposed throughout marriage	1,130	30	2.65	128	11.33	74	6.55	937	82.92
	Exposed part of marriage	609	10	1.64	75	12.32	34	5.58	503	82.59
	Unexposed part of marriage	775	10	1.29	82	10.58	27	3.48	667	86.06
	Unexposed throughout marriage	1,226	20	1.63	133	10.84	62	5.06	1,036	84.50
	All exposed	1,739	40	2.30	203	11.67	108	6.21	1,440	82.81
	All unexposed	2,001	30	1.50	215	10.74	89	4.45	1,703	85.11
	Total	3,740	70	1.87	418	11.18	197	5.27	3,143	84.04
2	Exposed throughout marriage	924	20	2.16	126	13.64	53	5.74	747	80.84
	Exposed part of marriage	863	30	3.48	113	13.09	51	5.91	702	81.34
	Unexposed part of marriage	342	6	1.75	37	10.82	17	4.97	289	84.50
	Unexposed throughout marriage	991	24	2.42	118	11.91	50	5.05	826	83.35
	All exposed	1,787	50	2.80	239	13.37	104	5.82	1,449	81.09
	All unexposed	1,333	30	2.25	155	11.63	67	5.03	1,115	83.65
	Total	3,120	80	2.56	394	12.63	171	5.48	2,564	82.18
3	Exposed throughout marriage	511	18	3.52	77	15.07	33	6.46	402	78.67
	Exposed part of marriage	609	20	3.28	106	17.41	39	6.40	465	76.35
	Unexposed part of marriage	109	2	1.83	15	13.76	4	3.67	90	82.57
	Unexposed throughout marriage	568	16	2.82	83	14.61	32	5.63	453	79.75
	All exposed	1,120	38	3.39	183	16.34	72	6.43	867	77.41
	All unexposed	677	18	2.66	98	14.48	36	5.32	543	80.21
	Total	1,797	56	3.12	281	15.64	108	6.01	1,410	78.46
4 and over	Exposed throughout marriage	323	6	1.86	61	18.89	19	5.88	247	76.47
	Exposed part of marriage	492	6	1.22	80	16.26	25	5.08	389	79.07
	Unexposed part of marriage	49	—	—	4	8.16	2	4.08	43	87.76
	Unexposed throughout marriage	424	16	3.77	76	17.92	22	5.19	326	76.89
	All exposed	815	12	1.47	141	17.30	44	5.40	636	78.04
	All unexposed	473	16	3.38	80	16.91	24	5.07	369	78.01
	Total	1,288	28	2.17	221	17.16	68	5.28	1,005	78.03

same groupings described in the preceding section. These rates are presented according to birth order since parity (or other factors highly correlated with parity) is known to influence reproductive wastage and perhaps other elements in the reproductive performance of man. Further, the persons included in this report have not all completed their reproductive span and, unless parity order or age of mother were taken into account, the pooling of all offspring might result in misinterpretations. In the breakdown of the material by birth order, several cells have only a few cases with a small number of total offspring. The rates resulting from such cells are most subject to errors inherent in dealing with small numbers.

It would appear that from the total of each parity order there is an increase in the number of twins in relation to total offspring as parity increases up to the fourth and higher groups, in which group the rate is again lower. Biologically, a

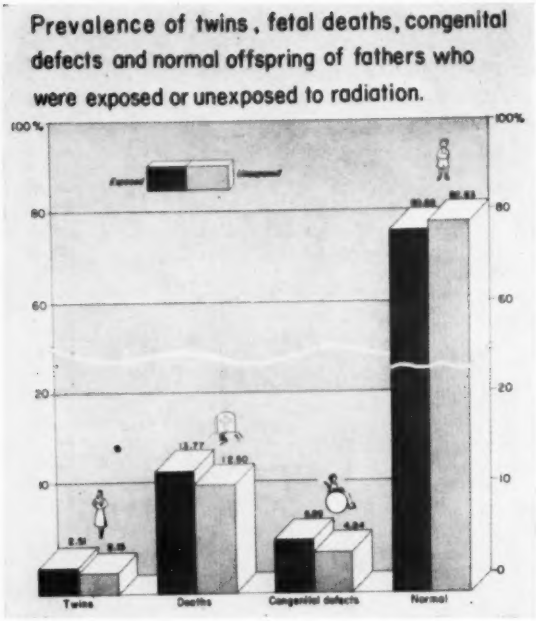

FIG. 6. Parity adjusted figures of Table XIII. The differences in the per cent of twins and per cent of fetal deaths are not statistically significant between the exposed and the controls. However, the differences in the per cent of congenital defects and per cent of normal births between the two groups *are* statistically significant.

more logical way of considering twins is in terms of the number of twin births per 100 pregnancies. Rates on this basis would be approximately half of those shown for twins in Table XII and a test of independence between parity order and twinning shows no statistically significant relationship at the 5 per cent level for this sample.

With increasing birth order the total fetal death rates increase from 11.18 per 100 in parity 1 to 17.16 per 100 in parities 4 and over. This progressive increase in the fetal death rate with increasing parity is statistically significant. Also significant is the decrease in the proportion of normal offspring with increasing birth order, a result which is to be expected in view of the relationships between fetal deaths and birth order. There is no statistical evidence from this study of any association between parity order and prevalence of congenital defects.

COMPARISON BETWEEN OFFSPRING OF EXPOSED AND UNEXPOSED PERSONS

Because of the influence of birth order on the proportion of affected offspring, together with disproportionate numbers of exposed and unexposed by birth order, the combined numbers of cases or unadjusted proportions of Table XIII are not comparable. In this section, therefore, whenever the significance of a difference between the totals of two exposure groups is mentioned, the difference tested is a combined difference weighted so as to take into account disproportions in parity order.

A weighted* average of the parity order differences and a weighted average of the variances of these differences is computed. The combined weighted difference divided by the square root of the combined variance determines the significance of the difference.

Considering first the "all exposed" with the "all unexposed" in Table XII, it is seen that the proportion of twin offspring in the exposed group exceeds that for the unexposed group in each parity except 4 and over. Rates for all parities combined and rates adjusted for differences in parity order are seen in Table XIII and Figure 6. The adjusted rates are those rates which would exist if each exposure group under consideration had the same parity distribution as the total population. For twins, for example, the observed proportion is 2.56 for all exposed fathers and 2.10 for all unexposed fathers. Because the all exposed group is different from the all unexposed group in

* The weight applied to the difference at each parity order is $w=\dfrac{1}{\dfrac{1}{k_1}+\dfrac{1}{k_2}}=\dfrac{k_1k_2}{k_1+k_2}$ where k_1 and k_2 are the numbers of offspring of exposed and unexposed persons. (See Snedecor, G. W. Statistical Methods, 1946, Chapters 11 and 17.)

The combined difference is $D=\dfrac{\Sigma w_i d_i}{\Sigma w_i}$.

The combined variance of this difference is $V(D)=\dfrac{\Sigma w_i^2 v(d)_i}{(\Sigma w_i)^2}$.

The variance of the difference at each parity is $v(d_i)=\dfrac{p_i q_i}{w_i}$.

TABLE XIII

OBSERVED AND PARITY ADJUSTED PREVALENCE OF TWINS, FETAL DEATHS, CONGENITAL DEFECTS, AND NORMAL OFFSPRING OF PERSONS EXPOSED AND UNEXPOSED TO RADIATION

Classification of Offspring	Total Offspring	Twins			Fetal Deaths			Congenital Defects			Normal		
		No	Per cent of total	Adjusted per cent*	No.	Per cent of total	Adjusted per cent*	No.	Per cent of total	Adjusted per cent*	No.	Per cent of total	Adjusted per cent
Fathers were exposed throughout marriage	2,888	74	2.56	2.57	392	13.57	13.69	179	6.20	6.20	2,333	80.78	80.67
These were born during and after fathers' exposure	2,573	66	2.57	2.46	374	14.54	13.86	149	5.79	5.74	2,059	80.02	80.73
These were born prior to fathers' exposure	1,275	18	1.41	1.53	138	10.82	11.74	50	3.92	3.98	1,089	85.41	84.21
Fathers were unexposed throughout marriage	3,209	76	2.37	2.38	410	12.78	12.79	166	5.17	5.17	2,641	82.30	82.28
All exposed	5,461	140	2.56	2.51	766	14.03	13.77	328	6.01	5.99	4,392	80.42	80.69
All unexposed	4,484	94	2.10	2.15	548	12.22	12.50	216	4.82	4.84	3,730	83.18	82.83
Total	9,945	234	2.35	2.35	1,314	13.21	13.21	544	5.47	5.47	8,122	81.67	81.67

* The adjusted per cent is the per cent that would exist if all groups had the same parity distribution.

the proportion of offspring in each parity, these rates are misleading. When the two groups are made comparable with respect to parity order the rates are 2.51 and 2.15 for the exposed and unexposed respectively. In terms of total offspring the only statistically significant difference in twinning between exposed and unexposed is in parity 4 and over. No other birth orders of Table XII nor the total of Table XIII show significant twin difference at the 5 per cent level. Figures for the number of twin births per 100 pregnancies are not shown. However, these figures (as stated previously these are approximately half of the figures shown for per cent of twin offspring) have been calculated and reveal no statistically significant association with radiation exposure of the father, either in total or within any birth order.

Considering fetal death rates, Table XII reveals that the all exposed group exceeds the all unexposed group within each birth order. None of the differences are statistically significant. The higher rate of the all exposed is seen also in the totals of Table XIII, although the differences between rates is less marked when the totals are adjusted for parity order. When parity differences are taken into account, the association between fetal deaths and exposure is not statistically significant at the 5 per cent level, the value of P being 0.07. If one compares separately fetal deaths among offspring of persons exposed to radiation throughout marriage and persons unexposed throughout marriage, the differences in rates are not as large as for the all exposed. However, parity for parity and in total, those exposed throughout marriage had higher rates than those unexposed throughout marriage. For the totals of these groups, parity order differences being taken into account, a test of independence between exposure and fetal deaths shows no statistically significant association since P equals 0.11.

Turning to congenital defects, the prevalence of defects is higher in the all exposed group than in the all unexposed group within each birth order. The association between exposure and prevalence is

TABLE XIV

PREVALENCE OF TWINS, FETAL DEATHS, CONGENITAL DEFECTS AND NORMAL OFFSPRING OF EXPOSED AND UNEXPOSED PERSONS ACCORDING TO BIRTH DATE OF OFFSPRING

Birth Date of Offspring	Offspring of Persons:	Total Offspring	Twins		Fetal Deaths		Congenital Defects		Normal	
			No.	Per cent of total offspring	No.	Per cent of total offspring	No.	Per cent of total offspring	No.	Per cent of total offspring
to 1925	Exposed throughout marriage	185	6	3.24	25	13.51	5	2.70	155	83.78
	Exposed part of marriage	168	4	2.38	15	8.93	5	2.98	150	89.28
	Unexposed part of marriage	287	2	0.70	20	6.97	7	2.44	260	90.59
	Unexposed throughout marriage	211	—	0.00	16	7.58	3	1.42	192	91.00
	All exposed	353	10	2.83	40	11.33	10	2.83	305	86.40
	All unexposed	498	2	0.40	36	7.23	10	2.01	452	90.76
	Total	851	12	1.41	76	8.93	20	2.35	757	88.95
1925 to 1935	Exposed throughout marriage	408	14	3.43	47	11.52	24	5.88	340	83.33
	Exposed part of marriage	231	4	1.73	36	15.58	8	3.46	188	81.39
	Unexposed part of marriage	230	—	0.00	18	7.83	8	3.48	205	89.13
	Unexposed throughout marriage	366	6	1.64	42	11.48	17	4.64	308	84.15
	All exposed	639	18	2.82	83	12.99	32	5.01	528	82.63
	All unexposed	596	6	1.01	60	10.07	25	4.19	513	86.07
	Total	1,235	24	1.94	143	11.58	57	4.62	1,041	84.29
1935 to 1945	Exposed throughout marriage	916	18	1.97	111	12.12	63	6.88	746	81.44
	Exposed part of marriage	752	24	3.19	98	13.03	43	5.72	612	81.38
	Unexposed part of marriage	564	14	2.48	73	12.94	24	4.26	468	82.98
	Unexposed throughout marriage	1,138	22	1.93	145	12.74	64	5.62	934	82.07
	All exposed	1,668	42	2.52	209	12.53	106	6.35	1,358	81.41
	All unexposed	1,702	36	2.12	218	12.81	88	5.17	1,402	82.37
	Total	3,370	78	2.31	427	12.67	194	5.76	2,760	81.90
1945 to 1952	Exposed throughout marriage	1,379	36	2.61	209	15.16	87	6.31	1,092	79.19
	Exposed part of marriage	1,415	34	2.40	220	15.55	93	6.57	1,107	78.23
	Unexposed part of marriage	194	2	1.03	27	13.92	11	5.67	156	80.41
	Unexposed throughout marriage	1,494	48	3.21	207	13.86	82	5.49	1,207	80.79
	All exposed	2,794	70	2.51	429	15.35	180	6.44	2,199	78.70
	All unexposed	1,688	50	2.96	234	13.86	93	5.51	1,363	80.75
	Total	4,482	120	2.68	663	14.79	273	6.09	3,562	79.47

significant at birth order 1 but not for higher birth orders in this study. However, in the totals of Table XIII, obtained by adding the defects and number of offspring of Table XII, the prevalence of defects of the all exposed group is significantly higher than the prevalence of the all unexposed group. It will be noted that since the rate of congenital defects is not strongly associated with birth order in this study, parity order adjustments result in only small changes in the prevalence differences between any two groups.

Again, when one compares the rate of defects of persons exposed throughout marriage with those unexposed throughout marriage (the groups least likely to be affected by possible nonreponse bias), the exposed have the higher rate at each birth order, but in no case significantly higher. When all birth orders are combined in Table XIII for these two groups, a test of independence of prevalence of defects and exposure results in a value of P of 0.08, showing no association at the 5 per cent level of significance.

Normal offspring include twins who were born alive and had no defects. The normal are therefore all offspring who were not classified as fetal deaths, congenitally defective, or both. Comparing the all exposed with the all unexposed, the former group has lower normal rates at each parity order. For parity order 1 the value of P is 0.05 and for parity order 2 the value is 0.06. The other parity orders are clearly not significant in the association between normal offspring and exposure. In Table XIII the difference between the proportion of normal offspring of exposed and unexposed persons is statistically significant. Comparing normal offspring of persons who were exposed throughout marriage with those unexposed throughout marriage, again the former group has the lower proportion normal, birth order for birth order, and in total. The differences are not significant for any parity order, nor for the total in which the value of P is 0.07.

Comparisons between the several groups when made according to age of the mother at time of birth of the offspring result in findings almost identical to those described above for parity order.

CHRONOLOGICAL CHANGES IN PROPORTION OF DEFECTS

Since physicians of all ages were included in this survey, dates of birth of offspring cover many years. During that time improvements in protection against radiation hazards have reduced the amount of radiation received per exposure. At the same time radiologists now do a greater volume of work, thereby increasing the dangers from cumulative exposure. Table XIV shows the proportion of normal and abnormal offspring among the several groups according to date of birth of offspring.

The more recent the date of birth, the higher are the proportions of twins, fetal deaths, and congenital defects, and the lower the proportion of normal offspring. With but few irregularities this is true within both exposed and unexposed groups alike; a finding which indicates that memory plays an important part in reporting.

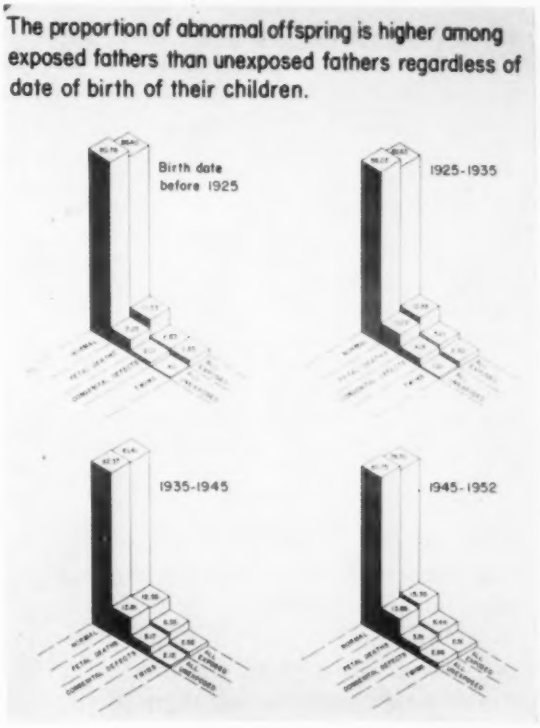
The proportion of abnormal offspring is higher among exposed fathers than unexposed fathers regardless of date of birth of their children.
Birth date before 1925
1925-1935
1935-1945
1945-1952

FIG. 7

For example, among persons who were exposed throughout marriage the proportion of normal offspring reported decreased from 91.00 per cent of children born prior to 1925 to 78.98 per cent of children born after 1945. Since this cannot be attributed to effects of radiation because a similar effect is noted in the unexposed group, it is quite probably due to forgetfulness of miscarriages or minor congenital defects in the earlier years. The effect of memory is so pronounced as to make it impossible to determine whether chronological changes due to radiation exposure have taken place. For the "all exposed" and "all unexposed" groups the association of normal, fetal deaths, and congenital defects with year of birth is in each case significant below the 0.05 level. The association of twins and year of birth is significant for the "all unexposed" but not for the "all exposed." Although the same pattern exists for the groups that were "exposed throughout marriage" and "unexposed throughout mar-

TABLE XV

NUMBER OF OFFSPRING AND PERSON-YEARS OF RISK OF HAVING OFFSPRING ACCORDING TO AGE OF WIVES OF EXPOSED AND UNEXPOSED PERSONS

Age of Wife	Exposed Throughout Marriage		Exposed Part of Marriage		Unexposed Part of Marriage		Unexposed Throughout Marriage	
	Person-years	No. of offspring	Person-years	No. of offspring	Person-years	No. of offspring	Person-years	No. of offspring
-24	961.50	284	456.00	190	1,678.25	347	1,399.00	362
25-29	3,635.50	1,063	2,896.00	934	3,017.75	602	4,571.25	1,256
30-34	4,538.50	1,041	4,274.00	960	1,542.00	265	4,851.25	1,074
35-39	3,601.75	414	3,735.00	392	568.50	58	3,484.00	430
40-46	3,014.00	86	3,312.50	97	174.75	3	2,537.25	87
All	15,751.25	2,888	14,673.50	2,573	6,981.25	1,275	16,842.75	3,209

riage," the association with year of birth is statistically significant only for the proportion of normal offspring in the latter group.

Again in Table XIV and in Figure 7 within each year of birth class, the proportion of normal offspring of the "all exposed" group is less than the proportion of normal of the "all unexposed" group (86.40 and 90.76 respectively prior to 1925, 82.63 and 86.07 from 1925 to 1935, 81.41 and 82.37 from 1935 to 1945, and 78.70 and 80.75 after 1945). With few exceptions the proportions of twins, fetal deaths, and congenital defects is higher, birth decade by birth decade, in the "all exposed" as compared to the "all unexposed." This picture exists also for offspring of persons exposed throughout marriage as compared to offspring of persons unexposed throughout marriage. For the large part these differences between exposed and unexposed within the several year-of-birth classes are not statistically significant, but they are uniform in direction throughout the years covered.

FERTILITY

Fertility is related to absolute age of the parents, age of marriage, and duration of marriage, all of which are in turn interrelated. Social factors also play a large role in fertility differences. In this report it is not possible to assess differences due to economics or employment of contraceptive methods. Although the groups selected for study are fairly homogeneous in some respects, such as education, there may be other factors for which there are differences between or within groups. In order to take biological factors into consideration, fertility is expressed here as the number of offspring per hundred person years of exposure to risk of having offspring within each five year age group of wives. Table XV gives the basic data upon which the rates of Table XVI are based. The number of person-years are determined as follows:

(a) For each full year that a wife is within the specified age group, she contributes one person-year of exposure to the total of that group.

(b) During the first year following marriage, a wife contributes only one-quarter of a person-year. The number of women who would have given birth to full term offspring during the first nine months of marriage is small.

(c) As a husband who was in an unexposed radiation group entered as exposed group, the wife was dropped from the risk of having her offspring in the unexposed group and picked up in the exposed group according to her age at the time.

(d) As a wife died or was otherwise separated from her husband she ceased to contribute to the person-years of exposure as of her age at that time.

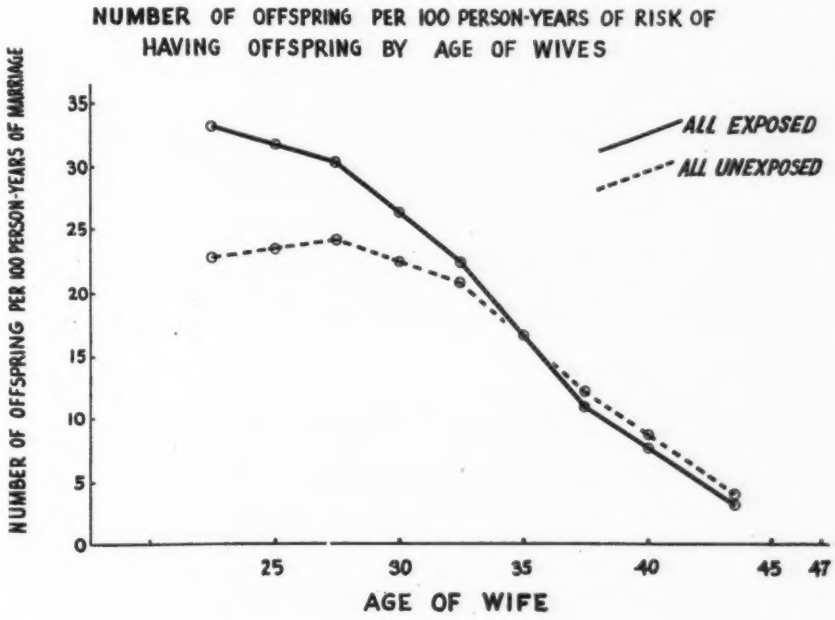

Fig. 8.

(e) As a wife reached age forty-six (actually 46.5) she was considered as no longer subject to the risk of having offspring, and tallied as having left the experience.

Calculation of years of exposure to risk of having offspring was not based on an individual tally of years and months of age at the time of entering and leaving the experience, since on most questionnaires month of birth, marriage, divorce, entry into radiation exposure and so on were not given. Rather the method was followed of assuming that a group of women entering the population during a certain year of age were evenly distributed throughout that year of age and therefore such a group contributes on the average only one-half of a year of exposure per person (with the exception pointed out in (b) above, where entry into the experience resulted from marriage). Similarly each person leaving the experience contributes one-half a person-year of exposure during the age at which she leaves. Person-years of risk were computed by single years of age and were then summed by five year age groups as shown in the tables. Offspring were tabulated according to the age of the mother at the time the birth occurred. It was found that the pattern of fertility for the exposed groups shows a higher fertility at ages less than thirty-five than for the unexposed group in these same ages. After the age of thirty-five the fertility of the exposed group is slightly lower than that of the unexposed groups (Fig. 8). For all exposed versus all unexposed the difference in the fertility pattern with age between the two groups is statistically significant.

The wives of those who were exposed throughout marriage when compared with the wives of those who were unexposed throughout marriage show the same age pattern of fertility as discussed above. However, the differences are not as marked and are not statistically significant.

It has been suggested that such things as the following may possibly play a role in creating the above findings:

1. Radiologists, considering the possible effects of prolonged exposure to radiation, may wish to have their children earlier.

2. Some radiologists may possibly achieve a higher economic level earlier than some of the other specialists. The economic "effect" may thus play a part.

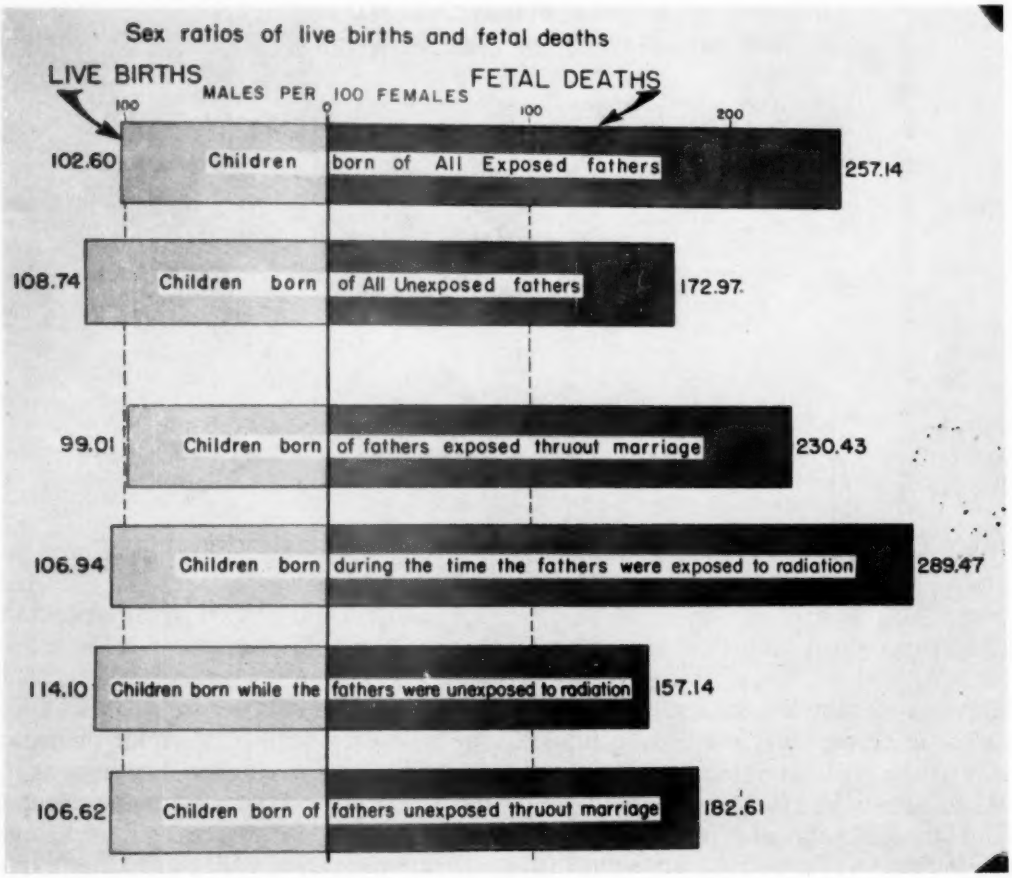

FIG. 9

3. Radiation effects may possibly increase fertility in the earlier years and cause the decrease only in later years.

4. Radiologists having had the number of children they want in the early years, may purposefully limit the number of children after the early years (33 children per 100 person-years at age 24 of wife for exposed, and 23 per 100 for unexposed, compared to 11 children per 100 person-years at ages 35–39 for exposed and 12 per 100 for unexposed).

In summary, the exposed group reported more offspring (21.19 offspring per 100 person-years of marriage) than the unexposed group (19.19 offspring per 100 person-years of marriage). This finding is opposite to that which one would expect from the results of past animal experiments.

RATIO OF MALE TO FEMALE BIRTHS

Table XVII and Figure 9 may be subject to considerable error due to the large number of live births of unstated sex, and fetal deaths of unstated or unknown sex. Although there is no reason to suspect that any group, because of greater or lesser degree of radiation exposure would be biased toward deliberately reporting (or failing to report) more males or females, the figures must nevertheless be viewed with caution.

The total sex ratio of 105.33 for live births of known sex is close to that of live births for this country. The sex ratio of males to females of live born children of exposed fathers is lower (fewer males per hundred females) than that of children of unexposed fathers. However, the difference between the "all exposed" and the "all

TABLE XVI

NUMBER OF OFFSPRING PER 100 PERSON-YEARS OF RISK OF HAVING OFFSPRING ACCORDING TO AGE OF WIVES OF EXPOSED AND UNEXPOSED PERSONS

Age of Wife	Offspring per 100 Person-Years of Marriage						
	Exposed throughout marriage	Exposed part of marriage	Unexposed part of marriage	Unexposed throughout marriage	All exposed	All unexposed	Total
–24	29.54	41.67	20.68	25.88	33.44	23.04	26.32
25–29	29.24	32.25	19.95	27.48	30.57	24.48	27.30
30–34	22.94	22.46	17.19	22.14	22.71	20.94	21.97
35–39	11.49	10.50	10.20	12.34	10.99	12.04	11.36
40–46	2.85	2.93	1.72	3.43	2.89	3.32	3.02
All	18.34	17.54	18.26	19.05	17.95	18.82	18.33
Adjusted	19.31	19.87	13.96	18.64	21.19	19.19	18.33

unexposed" ratio is within the limits of chance occurrence. This is true also of differences between sex ratios of live births among the other groups shown. Adjustment for differences in parity among the several groups results in minor changes which do not effect the relationships shown.

The sex ratios of fetal deaths, shown in the last column of Table XVII, are higher than those generally observed in official statistics or in special studies. This may result from the method of collection of these data, although all information on the sex ratio of fetal deaths suffers from large numbers of offspring of unknown sex and inaccuracy of sex determination of embryos and early fetuses.

The fetal death sex ratios of the exposed groups are higher than those of the unexposed groups. Although the differences are in no case statistically significant, it is of interest that this relationship is the inverse of that found for live births. An inverse relationship is to be expected if, as has been asserted, the live birth sex ratio is decreased by an increase in loss of males during fetal life. Males are lost at a higher rate than females under many conditions which adversely affect viability of the fetus.

Table XVIII shows no significant association between radiation exposure of the father and sex ratios of defective offspring. The total ratio of 133.33 is, however, significantly higher than that of all live born offspring.

TABLE XVII

SEX RATIOS OF LIVE BIRTHS AND OF FETAL DEATHS

Offspring of Persons:	Live Births				Fetal Deaths			
	Males	Females	Unknown	Males per 100 Females	Males	Females	Unknown	Males per 100 Females
Exposed throughout marriage	1,104	1,115	293	99.01	53	23	316	230.43
Exposed part of marriage	986	922	299	106.94	55	19	300	289.47
Unexposed part of marriage	526	461	152	114.10	22	14	102	157.14
Unexposed throughout marriage	1,240	1,163	404	106.62	42	23	345	182.61
All exposed	2,090	2,037	592	102.60	108	42	616	257.14
All unexposed	1,766	1,624	556	108.74	64	37	447	172.97
Total	3,856	3,661	1,148	105.33	172	79	1,063	217.72

TABLE XVIII

SEX RATIOS OF DEFECTIVE OFFSPRING

Offspring of Persons:	Defective Offspring			
	Males	Females	Unknown	Males per 100 Females
Exposed throughout marriage	91	72	16	126.39
Exposed part of marriage	71	53	25	133.96
Unexposed part of marriage	21	23	6	91.31
Unexposed throughout marriage	89	56	21	158.93
All exposed	162	125	41	129.60
All unexposed	110	79	27	139.24
Total	272	204	68	133.33

SUMMARY

1. Questionnaires were sent to 3,751 radiologists and to 3,858 other specialists (controls); 74.1 per cent of the radiologists and 53.8 per cent of the controls returned their questionnaires.

2. Male radiologists responded more readily than female radiologists (74.3 per cent to 66.7 per cent). Female controls responded slightly better than male controls (57.6 per cent to 53.5 per cent).

3. Radiologists as a group were slightly older than nonradiologists. Both groups showed the greatest response from those individuals in the thirty-nine to forty-eight year old age group. Older radiologists responded better than older controls.

4. Within both groups, persons with offspring responded most readily; those without offspring somewhat slower; and single persons least readily.

5. Those who failed to return a first questionnaire were sent a second questionnaire. Responses to first and second questionnaires showed no indication of interest bias due to family size.

6. All radiologists had worked with radiation-producing equipment. Among the controls it was found that 19.3 per cent had received frequent exposure in operating rooms (hip nailing, arteriography, angiocardiography, etc.). The returns indicated greater interest on the part of this group in the study than in the remainder of the controls.

7. Both the radiologists and the controls who responded were very nearly the same in proportions of married persons, persons with offspring and single persons. Among those who had offspring there were the same number of offspring per person among the radiologists (2.69) as among the controls (2.67).

8. In 5,461 offspring of radiologists and exposed controls there were 2.56 per cent twins, 14.03 per cent fetal deaths and 6.01 per cent congenital defects. In 4,484 offspring of unexposed controls there were 2.10 per cent twins, 12.22 per cent fetal deaths and 4.82 per cent congenital defects. Normal offspring constituted 83.23 per cent of the unexposed group as compared to 80.42 per cent normal offspring of the exposed group.

9. Three hundred and forty-eight congenital defects were reported in 328 offspring who had defects who were born of exposed fathers (6.01 per cent); 229 congenital defects were reported in 216 offspring who had defects who were born of unexposed fathers (4.82 per cent). These congential defects were classified according to the Manual of International Statistical Classification of Diseases, Injuries and Causes of Death. There were all types of defects reported. They involved the cardio-

vascular system, the blood, the respiratory tract, the muscles and joints, the cartilage and skeletal system, the gastrointestinal and genitourinary tracts, the central nervous system, the sensory organs and the endocrine system. There were 88 neoplasms reported in the 577 defects; 56 of these (1.03 per cent of total exposed offspring) were in the exposed group and 32 (0.71 per cent of total unexposed offspring) were in the unexposed group. The type and number of congenital defects and neoplasms are presented in table form.

Anomalies of the sense organs occurred with greatest frequency among both the exposed and the unexposed groups, representing 17.53 per cent and 18.34 per cent respectively of all anomalies reported.

Exposed persons reported a significantly higher proportion of heart, blood vesssel and blood anomalies (total of 14.37 per cent) than the unexposed persons reported (total 7.86 per cent). Unexposed persons reported a significantly higher proportion of muscle and joint defects (13.10 per cent to 7.47 per cent).

10. When the first questionnaire was not returned a second one was sent. An analysis of the returns indicates that for those groups that were exposed for part of their marriage there was possibly a bias toward reporting defects that occurred during the exposed portion of their marriage. Those groups who were exposed throughout their marriage and those who were unexposed throughout their marriage both showed a reticence to report abnormal offspring in response to the first questionnaire.

11. The two groups (those exposed throughout marriage and those unexposed throughout marriage) were similar with respect to parity of offspring and ages of the mother at the time the offspring were born.

12. In all offspring the percentage of twins increases as the parity order increases through parity 3, though there is no statistically significant relationship at the 5 per cent level for this sample. Comparison between exposed and unexposed groups also shows no statistically significant differences in rates of twinning.

13. The percentage of fetal death rates for all offspring increased from 11.18 per cent in parity 1, to 17.16 per cent in parities 4 and over. This progressive increase with increasing parity is a statistically significant increase in fetal death rates. Comparison of the fetal death rates of the offspring in the exposed group with those offspring in the unexposed group shows the exposed group to have the higher rates at every parity but the differences are not statistically significant at any parity or in total.

14. The percentage of congenital defects is higher in the all exposed group than in the all unexposed group at each parity level. However, it is statistically significant only at the parity 1 level. The adjusted totals of all parities show 5.99 per cent congenital defects among the 5,461 exposed offspring as compared to 4.84 per cent defects among the 4,484 unexposed offspring. This is a statistically significant figure (P equals 0.01).

15. The percentage of normal offspring is lower in the all exposed group than in the all unexposed group (80.59 per cent to 82.83 per cent). This too, is a significant level (P equals 0.01).

16. When the offspring of persons exposed throughout marriage are compared with the offspring of persons unexposed throughout marriage the trend in all variations from normal is similar to the differences described in the above paragraphs although for the most part these differences are not statistically significant.

17. The farther back in the past that births occurred as reported in the questionnaires in this survey, the less the respondents remembered concerning the occurrence of variations from normal in their offspring. This is observed in the completed questionnaires of both exposed and unexposed groups.

18. The pattern of fertility for the exposed group is higher at ages less than thirty-five than for the unexposed group up to this age. After age thirty-five the fertility

pattern of the exposed group is slightly lower than that of the unexposed group.

19. Among the exposed fathers there were fewer live males born per hundred live female births. However, the difference is not a statistically significant one and could possibly be a chance occurrence. There were more dead males than dead females reported born to the exposed group, but this, too, must be considered as only a trend because the difference is not a statistically significant one.

CONCLUSION

Comments received on questionnaires sent to radiologists and nonradiologists indicate a wide difference of opinion on the possible effects of relatively small but frequent doses of ionizing radiation on the offspring of exposed fathers. The data given in the body of the above paper present a picture of first generation effects.

With consideration for possible biases and particularly considering the differences between offspring of fathers who were exposed throughout marriage and fathers who were unexposed throughout marriage, the results indicate that small prolonged doses of radiation produce abnormalities in humans. The differences between exposed and unexposed groups show a consistent trend of higher rates of abnormality in the exposed group within the several parity orders, ages of mother, and decades of birth of offspring.

The differences are not of large magnitude and in themselves would not be viewed with alarm. These abnormalities occur, however, in the *first generation* of offspring and visible first generation effects represent only a small fraction of the total damage that may have been inflicted.

Study of the effects of radiation should not be based only upon defects so gross that they are lethal or make it improbable that the affected person would ever reproduce. Therefore, minor defects are included in this report as well as the more serious ones. Gross defects, while they are an immediate burden in any generation, are not nearly so costly as minor defects transmitted over a very long span of time.

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Credit for technical and secretarial help is gratefully given to: Mrs. Katherine Burtner, Miss Louise Cline, Mrs. Catherine Fiorio, Mrs. Naomi Macht, Mrs. Marjorie Nalley, Miss Louise Rohrer and Mrs. Dorothy Zinkand.

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A COMPARISON OF FETAL AND INFANT DEATH RATES IN THE PROGENY OF RADIOLOGISTS AND PATHOLOGISTS*

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THIS study was undertaken to determine whether or not the fetal and infant death rates are detectably different in the families of radiologists than they are in those of comparable groups not working with ionizing radiations. From the data on experimental animals only a very small fraction of genetic effects of radiations would be expected to appear in the immediate offspring of exposed fathers and only a small proportion of the total genetic damage would be manifest as fetal and infant deaths. Therefore, even if the genetic damage due to radiations were considerable, a study of miscarriages in the wives and early deaths in the children of exposed persons might fail to detect it. Nevertheless, it seemed worth while to see if any such effects could be found.

In August, 1951, 1,027 questionnaires were mailed to radiologists and 1,036 to a control group of pathologists chosen from the Directory of Medical Specialists. After the questionnaires had been mailed, it was learned that a similar study was being conducted by Macht and Lawrence.[1] Because their questionnaires were more detailed and were sent to a larger number of persons, publication of the results in this study was delayed until the analysis of Macht and Lawrence's data could be completed.

The data in this paper agree with those of Macht and Lawrence in failing to show a statistically significant increase in stillbirths and miscarriages among the wives of radiologists. However, since many physicians must have answered both questionnaires, the two studies cannot be regarded as providing independent data.

The procedure of this study differed from that of Macht and Lawrence in one important respect. Whereas these investigators carefully explained the purpose of their study in their covering letter, the brief letter covering questionnaires in this study simply solicited the physicians' cooperation in completing the questionnaire without telling him the purpose of the study. It was thought this might help to avoid a biased response. Because of this methodological difference it seems worth while to add the additional data thus obtained to the record.

The letter and questionnaire are shown in Figures 1 and 2.

RESPONSE OF RADIOLOGISTS AND PATHOLOGISTS

The response data are given in Table 1. No attempt was made to arrange the procedure so as to make possible a follow-up for those who did not respond to the first letter; the anonymity of responders was preserved even to the extent of the author having no way of identifying which physicians had replied.

TABLE I

RESPONSE TO QUESTIONNAIRE BY RADIOLOGISTS AND PATHOLOGISTS

	Radiologists	Pathologists
Total questionnaires sent	1,027	1,036
Wrong address, deceased, etc.	62	64
Completed and returned	682	589
Per cent returned	70.7	60.6

* Paper number 472 from the Department of Genetics. This work was aided by a grant from the Research Committee with funds provided by the Wisconsin Alumni Research Foundation.

Dear Doctor:

As part of a research project, I would like to get certain information about radiologists, pathologists, and other medical specialists. I am fully aware of the annoyance created by excessive questionnaires, but in this case it seems to be the only feasible way of getting the necessary data. If you would be willing to cooperate, would you please fill out and return the enclosed sheet? As you can see it is very brief and for your convenience, a stamped addressed envelope is enclosed.

Thank you very much for your help.

Very truly yours,

Richard Weiner

Richard Weiner

P. S. If you are retired, please fill out the questionnaire anyhow.

Fig. 1. The letter sent out with the questionnaires.

Only data from married males were used in the analysis. Questionnaires from radiologists who worked primarily in other fields and from pathologists who did any roentgen-ray work were excluded. Three questionnaires were improperly answered. There remained 530 from pathologists and 655 from radiologists. These form the basis for the following findings.

Tables II and III show the very similar distribution of age of respondents and number of their children.

FETAL AND INFANT DEATHS

Each respondent was asked for the number of miscarriages and stillbirths in his wife's history; for the number of children born alive who had since died, with the age of death of each. Miscarriages and stillbirths are pooled in this analysis. Infant deaths comprise children born alive who died within the first year. Induced abortions are not included. A twin miscarriage is counted as one. Unlike the investigation of Macht and Lawrence, information on congenital malformations was not requested.

The data (Table IV) show no significant differences between the two professional groups. The chi-square value for the distribution of total deaths (infant and fetal) is 7.5 with 5 degrees of freedom (the groups with 5 or more were pooled), leading to a probability of 0.2. The uncorrected fetal death rates in the radiologist and pathologist groups (0.166 and 0.159) are very similar. A difference of about 0.037 would be required for 5 per cent statistical significance. The infant death rates are also very similar, but are based on such small numbers as to have very little meaning.

DISCUSSION

The data given here are in agreement with

Table II

AGE DISTRIBUTION OF RESPONDENTS

	Radiologists		Pathologists	
	Frequency	Per cent	Frequency	Per cent
35 or less	23	3.5	17	3.2
36–45	262	40.1	225	42.4
46–55	186	28.4	160	30.2
56–65	130	19.9	92	17.4
66 and over	53	8.1	36	6.8
Total	654	100.0	530	100.0
Average age	49.30		48.50	

1. What is your medical specialty? _____
2. How many years have you been engaged in this specialty? _____
3. How old were you at your last birthday? _____
4. What year were you married? (If married more than once, write year of first marriage.) _____
5. How many children have you had? (Include those who were born alive, but have died since.) _____
6. Please indicate the ages of children now living. _____
7. How many children born alive have died since? _____
8. Please indicate the age of death and, if known, the cause for each child who has died since birth.
9. How many miscarriages has your wife had? _____
10. Please indicate the approximate foetal age and cause, if known, of any miscarriages
11. How many stillbirths has your wife had? _____
12. Please indicate the causes and pathological details, if known, of any stillbirths.
13. Do you ever use a fluoroscope? _____
14. If yes, for how many hours per week? ____ for how many years? _____
15. Do you routinely handle radium, radon, or other radioactive substances? _____
16. Do you routinely operate an X-ray machine for purposes other than fluoroscopy? _____
17. Has your wife at any time engaged in X-ray work? _____
18. If yes, for how many years? _____

(Optional) Please supply on the reverse any additional relevant information.

FIG. 2. The questionnaire sent to radiologists and pathologists.

those of Macht and Lawrence in failing to show a statistically significant difference in the fetal death rates in the two groups. The sample in this study had more families with many stillbirths and miscarriages among the radiologist group than among the pathologist group (9 with 5 or more deaths as compared with 2), but this difference is also not statistically significant.

The over-all fetal death rate in this study is significantly higher ($P < 0.01$) than that found by Macht and Lawrence (16.3 per cent vs. 13.2 per cent). This may be attributed to the greater age of our sample (*cf.* Table II with Macht and Lawrence's Table III). Our mailing list was prepared from an older edition of the Directory so as to give a larger number of completed families. Macht and Lawrence have shown a lower frequency of fetal deaths in first

TABLE III

DISTRIBUTION OF NUMBER OF LIVE BIRTHS PER FAMILY

Number of Live Births	Radiologists		Pathologists	
	Frequency	Per cent	Frequency	Per cent
0	100	15.3	75	14.2
1	97	14.8	67	12.6
2	225	34.4	195	36.8
3	142	21.7	130	24.5
4	69	10.5	43	8.1
5+	22	3.4	20	3.8
Total	655	100.1	530	100.0
Total live births	1,379		1,133	
Live births per family	2.11		2.14	

TABLE IV

DISTRIBUTION OF FETAL AND INFANT DEATHS IN THE PROGENY OF MALE RADIOLOGISTS AND PATHOLOGISTS

Number of Deaths	Frequency in Radiologists		Frequency in Pathologists	
	Fetal	Infant	Fetal	Infant
0	498	638	391	512
1	99	12	90	17
2	33	4	32	1
3	8	1	10	
4	7		5	
5	4		1	
6	3		1	
7	2			
"Several"	1			
Total	655	655	530	530
Total pregnancy terminations	1,653		1,348	
Total fetal deaths	274		215	
Total live births	1,379		1,133	
Total infant deaths	23		19	
Infant deaths per live birth	0.0167		0.0168	
Fetal deaths per pregnancy	0.1658		0.1595	
Fetal deaths per family	0.4183		0.4057	

and second pregnancies, which would be more frequent in their data than in this study.

Data on fetal deaths are, of course, subject to many errors. Early miscarriages are likely to be undetected or forgotten and variation with parity is another factor. For these and other reasons a small difference between the rates in the two professional groups might be due to causes other than radiation. From this study it appears that the amount of radiation received by radiologists under usual conditions does not have any very large effect on the total fetal and infant death rate in their children. However, Macht and Lawrence report a significant difference between families of radiologists and non-radiologists in normal pregnancy terminations (those not classified as stillbirths, congenital defectives, or both).

The genetic implication is another question. Studies with experimental animals have shown that only a very small fraction of genetic damage due to radiation appears in the first generation offspring, and in a form capable of detection in this type of study.[2,3] The lack of an overt effect on fetal and infant death rates may be due to this limitation or to the effectiveness of the cautionary measures against exposure to radiations on the part of the radiological profession. In any event, the negative or inconclusive findings in this study have little bearing on the question of over-all genetic damage to the human population in future generations.

SUMMARY

A questionnaire study showed no statistically significant differences between the frequencies of still births and miscarriages in the wives of radiologists (16.6 per cent) and in a control group of pathologist's wives (15.9 per cent). The infant mortality rates also were not significantly different in the children of the two groups, but the numbers were very small. It thus appears

that the amount of radiation received by radiologists under usual conditions does not have any very large effect on fetal and infant death rates in their children.

The problem of assessment of genetic effects is complicated by the fact that only a very small fraction of the total genetic damage would be detected as an increase in fetal and infant death rates in the first generation progeny. The negative results of this study are therefore regarded as having little bearing on the question of genetic hazards from exposure to radiation.

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Mr. Richard Weiner assisted in the preparation and mailing of the questionnaires.

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A VITAMIN C-FREE DIET IN RADIATION THERAPY OF MALIGNANT DISEASES*

By THEODORE R. MILLER, M.D.,† *and* BORIS SOKOLOFF, M.D.‡

NICHOL and Welch,[9] Broquist *et al.*,[2] and Sokoloff *et al.*[12] found that ascorbic acid greatly enhanced the conversion of folic acid into citrovorum factor, and that, on the other hand, low concentrations of vitamin C in the blood and tissue almost completely arrested this conversion. Since citrovorum factor, according to Farber and others, exerts a stimulating effect on certain malignant diseases, particularly those of the lymphatic system, many antifolic preparations were developed to combat leukemia and related diseases. On the basis that a vitamin C-free diet acts as a mild antifolic agent and prevents the formation of citrovorum factor, Sokoloff *et al.*[13] introduced this diet, combined with small doses of cortisone, for the treatment of chronic leukemia and related diseases.

More recent studies by Gol'dshtein *et al.*,[6] and Sokoloff *et al.*,[7,14,15,16] gave an indication that ascorbic acid takes an active part in the formation of desoxyribonucleic acid of nuclei and cells, a substance which is generally considered as being essential for the multiplication of malignant cells.

The question was naturally asked whether or not a vitamin C-free diet would induce a scurvy syndrome and thus confuse the results of the investigation. However, contrary to the prevalent opinion that a diet deficient or low in vitamin C unavoidably brings about a scurvy syndrome, Crandon *et al.*[4] demonstrated, in a clinical study of a large number of healthy persons, that man can be kept on a vitamin C-free diet without experiencing any signs of scurvy for 132 days. These workers observed that the plasma ascorbic acid concentration dropped to and remained at zero after forty-one days of the experimental vitamin C-free regimen, even though the abnormal clinical signs, such as hyperkeratotic papules, of ascorbic acid deficiency did not appear before 132 days. No change in the condition of the gums was noticed until after petechiae had appeared on the legs, following six months' subsistence on a virtually vitamin C-free diet. Similar observations were made by Burrill[3] and Stamm *et al.*[17] Miller *et al.*,[8] who kept their patients affected with malignant diseases on a vitamin C-free diet for from four to six months without any apparent signs of a scurvy syndrome, arrived at the conclusion that this regimen can be safely used in radiation therapy, without any danger of inducing scurvy.

The fact that low vitamin C concentrations in blood and tissue increase the fragility of the vascular system of a tumor bed, according to Eddy *et al.*,[5] and thus apparently makes it more radiosensitive (Francis Carter Wood) also served us as a biological premise to the present investigation.

EXPERIMENTAL

In our first series of experiments we took two groups of guinea pigs of the family 2.§ Each group consisted of 6 animals. Group I was placed on a Sherman-LaMer scorbutogenic diet. Group II was kept on the same diet plus daily injections of 40 mg. of sodium ascorbate. Twenty-four hours before these trials began,

§ We would like to express our gratitude to Dr. W. E. Heston of the National Cancer Institute for the generous supply of guinea pigs of family 2 and for the transplantable tumor, liposarcoma.

* Presented at the Seventh International Congress of Radiology, July, 1953, Copenhagen, Denmark; the annual meeting of the American Association for Cancer Research, April 12, 1952, New York City; and the annual meeting of the American Society for Experimental Pathology, April 15, 1952. Preliminary reports: *Cancer Research*, 1952, *12*, 284; *Cancer Research*, 1952, *12*, 298; *Fed Proc.*, 1952, *2*, 487; *Fed. Proc.*, 1952, *2*, 428.

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Aided by a grant from Damon Runyon Fund for Cancer Research.

liposarcoma was transplanted to the animals of the two groups. One animal of each group was killed after two weeks of diet.

The growth of liposarcoma in guinea pigs on a Sherman-LaMer scorbutogenic diet (Group I) was very slow and at the end of thirty days the average tumor weight was only 7.4 gm., while the tumors of guinea pigs receiving ascorbic acid averaged 26.5 gm. The ascorbic acid values of tumor tissue were: in Group I, 0.05 ∓0.022 mg/100 gm. tissue and in Group II, 23.25∓1.55 mg/100 gm. tissue. From these observations, it appears that a vitamin C-free diet retarded considerably the growth of liposarcoma, bringing down the ascorbic acid concentration of tumor tissue close to zero. This observation confirms the findings of Robertson *et al.*[11] of the National Cancer Institute concerning the effect of a scorbutogenic diet on the growth of fibrosarcoma in guinea pigs.

In our next series of experiments, the rats, bearers of Crocker carcinoma, a fast growing tumor which never receded, were placed on a scorbutogenic diet and submitted to roentgen irradiation. In order to bring down the ascorbic acid concentrations in blood and tissue close to zero, an analogue of ascorbic acid, 2,3-enediol-d-gluco-heptono-1.4-lactone, otherwise known as d-gluco-ascorbic acid, was added in an amount of 2 per cent to a Sherman-LaMer scorbutogenic diet. The addition of an analogue was imperative since rats synthesize ascorbic acid while men do not. A single dose of 3,000 r and 5,000 r was delivered. Radiation factors were: The Chaoul contact apparatus, 60 kv., 0.12 mm. Cu filter, 3 cm. distance from the target to the center, with the field 3 cm. and 450/min. measured by a Siemans dosimeter. The average size of tumors was 18 mm. in diameter.

Charts II–VI summarize the results of these trials.

Chart II represents the growth of Crocker carcinoma in rats kept on regular Purina ration and receiving no radiation. The tumors grew fast and the animals died on an average in thirty-five days. Chart III represents the growth of Crocker carcinoma in rats also kept

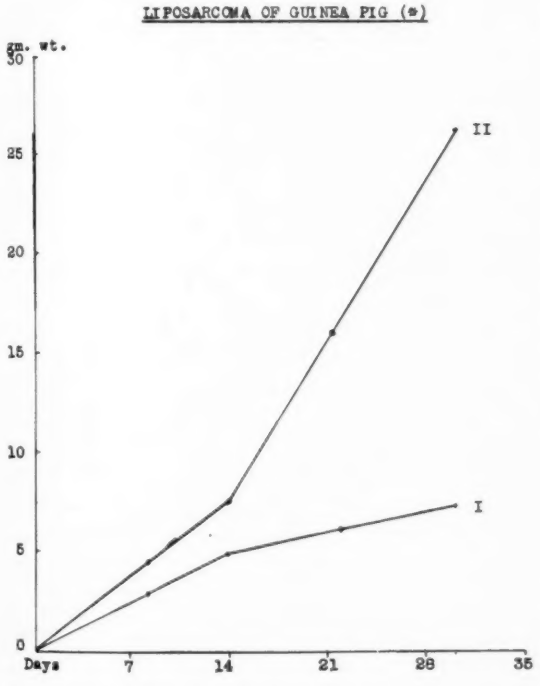

Chart I. (I) Average tumor weight of liposarcoma for 5 guinea pigs, kept for 30 days on a Sherman-LaMer scorbutogenic diet, is 7.4 gm.

(II) Average tumor weight of liposarcoma for 5 guinea pigs, kept for 30 days on a Sherman-LaMer scorbutogenic diet and receiving daily injections of 40 mg. of sodium ascorbate, is 26.5 gm.

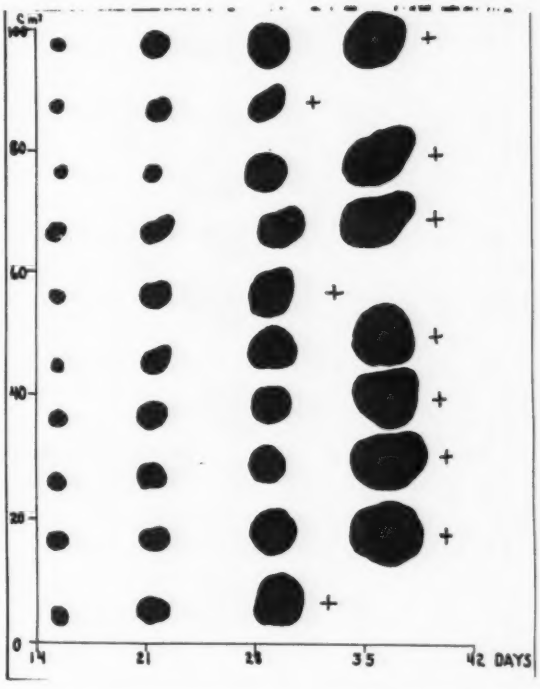

Chart II. Normal growth of Crocker rat carcinoma. Twenty rats, the average weight 180 gm., were kept on Purina Chow, 18 gm/day/rat. All rats died from cancer, with the average span of life of 35 days.

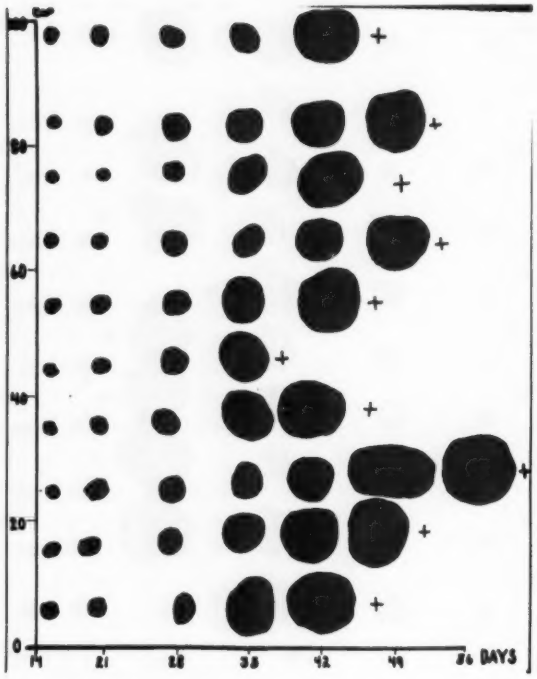

Chart III. Crocker rat carcinoma submitted to 3,000 r contact radiation in a single dose. Twenty rats, males, the average weight 183 gm., were kept on Purina Chow, 18 gm/day/rat. The average size of tumor when irradiated was 17.5 mm. in diameter. All rats died from cancer with an average span of life of 48 days.

on a Purina diet. Three thousand roentgens contact radiation in a single dose were delivered. Not a single tumor was completely destroyed but the growth was arrested temporarily. In the end, all rats died from cancer. The average span of life was forty-eight days.

Chart IV summarizes the figures concerning the growth of Crocker carcinoma in rats kept on a Sherman-LaMer scorbutogenic diet plus 2 per cent of d-gluco-ascorbic acid. They received 3,000 r contact radiation in a single dose. The ascorbic acid concentration was 0.01 mg. per 100 cc. of blood plasma at the time of irradiation. All rats survived and all tumors were destroyed.

Chart V represents the growth of Crocker carcinoma in rats kept on a regular Purina ration. They were given 5,000 r contact radiation in a single dose. There was a considerable retardation of tumor growth but no complete destruction was observed. Subsequently, all rats died from cancer. The average span of life was fifty-seven days.

Chart VI shows the growth of Crocker carcinoma in rats kept on a Sherman-LaMer scorbutogenic diet plus 2 per cent of d-gluco-ascorbic acid. They received 5,000 r contact radiation in a single dose. The ascorbic acid concentration was 0.015 mg. per 100 cc. of blood plasma at the time of irradiation. There was a prompt destruction of all tumors and all rats survived.

These results indicate that a regimen which brings the ascorbic acid concentrations in blood and tissue down close to zero apparently increases the radiosensitivity of Crocker rat carcinoma. Under normal conditions of diet, only 10,000 r contact radiation delivered in a single dose were able to destroy completely Crocker carcinoma of 18 mm. in diameter. Histological examinations of irradiated tissue revealed a much greater damage to the tumor vascular bed in treated animals than in controls. The lumens of the arterioles, meta-arterioles and capillaries were undetectable with numerous small hemorrhages and collagen degeneration present.

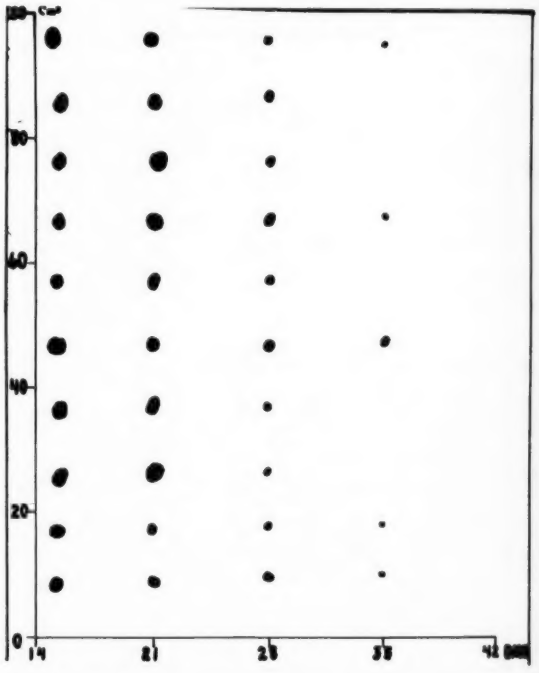

Chart IV. Crocker rat carcinoma submitted to 3,000 r contact radiation in a single dose. Twenty rats, males, the average weight 177 gm., were kept on a Sherman-LaMer scorbutogenic diet supplemented with 2 per cent of d-gluco-ascorbic acid, 19 gm/day/rat. The average size of the tumor when irradiated was 18.4 mm. in diameter. All rats survived with the tumors destroyed.

CLINICAL

Twenty-six patients with various types of malignant diseases were placed on a scorbutogenic diet from two to three weeks before conventional roentgen irradiation was applied to the tumors, during the whole course of irradiation, and for two to three months postirradiation period. In order to obtain the maximal salutary effect from this method, it was imperative to bring the ascorbic acid concentration of blood down to 0.05 mg/100 cc. blood plasma before the initial exposure to roentgen radiation. According to our investigation, it took about eighteen to twenty days on a strict vitamin C-free diet to accomplish such a reduction in the ascorbic acid level. Unfortunately, in a certain number of our cases, the pre-irradiation period of dieting was shorter and the ascorbic acid blood level in these patients at the time of initial roentgen-ray

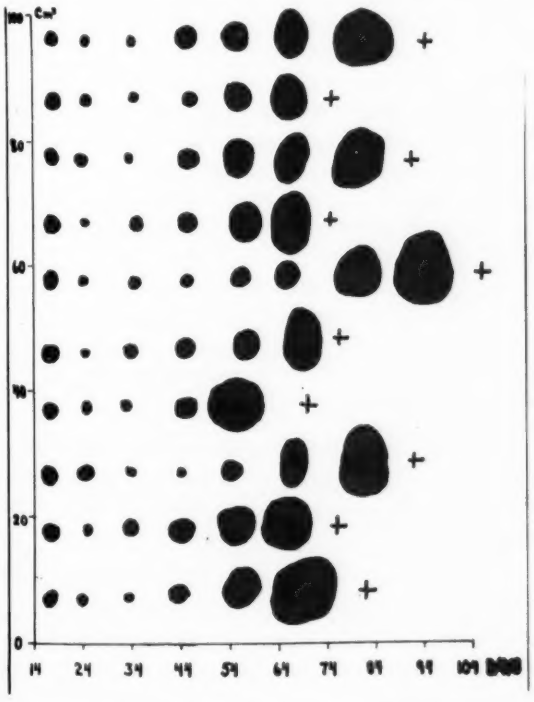

Chart V. Crocker rat carcinoma submitted to 5,000 r contact radiation in a single dose. Twenty rats, males, the average weight 188 gm., were kept on Purina Chow, 18 gm/day/rat. The average size of the tumor when irradiated was 17.4 mm. in diammeter. All rats died from cancer with an average span of life of 57 days.

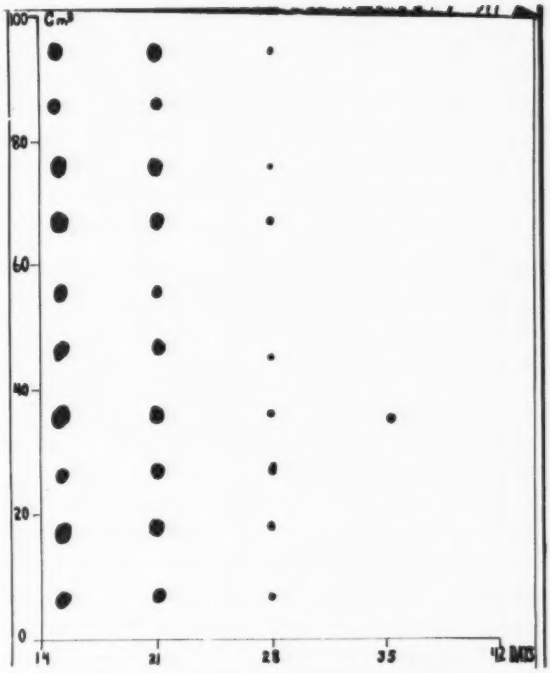

Chart VI. Crocker rat carcinoma submitted to 5,000 r contact radiation in a single dose. Twenty rats, males, the average weight 181 gm., were kept on a Sherman-LaMer scorbutogenic diet supplemented with 2 per cent of d-gluco-ascorbic acid, 19 gm/day/rat. The average size of the tumor when irradiated was 18.2 mm. in diameter. All rats survived with the tumors destroyed.

delivery was much higher, about 0.1–0.2 mg/100 cc. This might account for the fact that in these specific cases the results of therapy so obtained were less satisfactory. In order to increase the tolerance of the organism to radiation, bio-flavonoids (C.V.P.) were given, 6 capsules or 600 mg. per day, during the whole course of therapy.

Diet: The diet consisted of lean meats, poultry, fish, eggs, bread, flour, macaroni, small amounts of butter, prune juice, green olives, fresh prunes, nuts, cheese and ice cream. These products contain no vitamin C at all.[6] A glass of non-fortified apple juice might be given. It contains 2 mg. of vitamin C. Beets might be added to the diet since one cup of them contains less than 0.5 mg. of vitamin C.

No milk, liver or kidney was given. All fruits and vegetables were excluded from the diet (except prunes). The diet was

low in fat and high in proteins, altogether about 2,000–2,500 calories. This diet, containing no more than 5 mg. of vitamin C per day was well tolerated by patients and they remained on it for five to six months without any ill effect. In fact, their general well-being seemed to be better on this diet than on a balanced diet.

Our clinical investigations cover 11 cases of lymphosarcoma, 1 case of fibrosarcoma, 1 case of liposarcoma, 4 cases of Hodgkin's disease, 4 cases of teratoma of the testis, 1 case of hepatoma and 4 cases of generalized carcinomatosis.

Four cases of lymphosarcoma remained well after their initial treatment three years ago which was of the obliterative type. Five cases, also of the obliterative type, and which manifested a prompt recurrence after this first series of roentgen irradiation were placed on a scorbutogenic diet and submitted to a new series of irradiation. The response was very satisfactory, in fact much better than in the first series of radiation treatments when they were kept on a regular diet. These 5 cases have had further areas of treatment which responded satisfactorily to this regimen. In 2 well advanced cases of lymphosarcoma, the patients died before the method could be evaluated.

The case of fibrosarcoma was treated with good initial and permanent regression in the affected area. This patient remains in satisfactory condition with persistent but controlled disease for about three years.

This is the case of a thirty-six year old white woman with a history of having had a fibrosarcoma excised from the left iliac region in 1947. The tumor recurred in 1948 and was re-excised, having to be dissected of the external iliac artery. The patient remained well until the spring of 1950, when the tumor recurred in the left obturator fossa. The patient was advised that she should have a hemipelvectomy, but refused operation. She was placed on a vitamin C-free diet. After twelve days of a pre-irradiation diet, with the ascorbic acid level in blood going down to 0.02 mg. per 100 cc., she was given 4,200 r through a grid, with considerable regression in the tumor. Following the completion of roentgen therapy, she remained on a vitamin C-free diet for another three months, during which time the tumor continued to regress and remained stationary for twelve months when it began to increase slightly in size. Another series of irradiation was applied while she was kept on a vitamin C-free diet. Up to now, the growth remains in a stationary state.

In this case, we have a radioresistant tumor which responded favorably but not completely to irradiation.

The case of a liposarcoma is also indicative in this respect.

This patient was a fifty-seven year old white man, with a history of having a liposarcoma excised from the left calf about three years ago. Twelve months later, the patient developed pain and abdominal ascites. On exploration, he was found to have abdominal liposarcomatosis with friable implants throughout the abdomen. The patient was placed on a vitamin C-free diet and when the ascorbic acid level in the blood was brought down to 0.01 mg. per 100 cc. of plasma, he was given 3,600 r × 4 to the abdominal cavity using 1,000 kv. with 3.8 lead filter, in fractions of 300 r each, in thirty-six days. A vitamin C-free diet was discontinued two months after the irradiation series. There was good initial and permanent regression of lesions, the abdominal masses gradually disappeared to palpation and the ascites subsided. For more than a year there was no evidence of recurrence.

In this case, an apparently radioresistant tumor underwent a complete regression when the patient was kept on a vitamin C-free diet while receiving irradiation.

The group of patients affected with Hodgkin's disease deserves particular attention. In all 4 cases, the patients received conventional radiation therapy with prompt recurrence of the growth. When they were placed on a vitamin C-free diet and submitted to roentgen irradiation, the disease seemed to be much better controlled, and the patients remained free from all symptoms for fifteen to twenty months.

The following cases may illustrate this observation.

E.R., female, aged twenty-two, with a history of having a mass in the left apex discovered on routine chest roentgenogram in 1950. On examination, a small node was found in the left supraclavicular space and removed for biopsy. This proved to be Hodgkin's disease, and the patient was consequently given roentgen therapy. The apical mass disappeared but promptly recurred in two months. The patient was placed on a vitamin C-free diet for sixteen days and, when the blood ascorbic acid level was brought down to 0.02 mg./100 cc., a new series of roentgen irradiation was applied. The patient remained on a vitamin C-free diet for another three months, during which time she gained 10 pounds in weight. There was no sign of the disease for fifteen months when again a small apical tumor reappeared. Again the patient was placed on the diet and given roentgen irradiation with consequent control of the disease up to the present time.

I.B., white female, aged twenty-one, with a history of developing a mass in the left supraclavicular space, hard and fixed to the underlying structures. This followed the administration of typhoid vaccine. Biopsy revealed it to be a Hodgkin's granuloma. To roentgen therapy, the mass responded only partially with subsequent progress of the disease. The patient was placed for fourteen days on a vitamin C-free diet and submitted to a new series of roentgen treatments. At the time of the initial exposure, the blood ascorbic acid was found to be 0.03 mg./100 cc. This time the mass promptly disappeared and the patient remained well for a period of about fourteen months, when a sign of the recurrence of the disease was again observed. A new series of roentgen treatments were delivered while the patient was kept on a vitamin C-free diet. The disease seems to be under control.

K.B., white female, aged twenty-six, with a history of dyspnea and the discovery of a large mediastinal mass extending up to the right thyroid region. Biopsy revealed the condition to be Hodgkin's disease. The patient was given roentgen therapy with partial control of her disease for about three months, when she became pregnant. The disease then flared up, accompanied by a high temperature and much prostration. Therapeutic abortion was done and a new series of roentgen treatments was given without any improvement in the patient's condition. Three months later, when the patient was considered in a critical stage, she was placed on a vitamin C-free diet for twelve days. A new series was applied. At the time of the initial exposure, the blood ascorbic acid level was 0.05 mg./100 cc. The response to irradiation was much better this time and a large part of the malignant mass disappeared. The rate of progress of the disease was definitely slowed down to a considerable degree. The patient tolerated radiation therapy much better than in the first two series of roentgen treatments when she was kept on a non-restricted diet. For the last ten months, the disease has remained stationary.

The analysis of the cases of Hodgkin's disease treated with roentgen radiation and a vitamin C-free diet indicates that this method is not a complete solution for this condition. Nevertheless, one feels that by reducing the ascorbic acid concentration in the blood close to zero during the preirradiation, irradiation, and postirradiation periods, one is able to achieve a much better control of Hodgkin's disease and to obtain much longer periods of remission than with conventional treatment. There seems to be some indication that the preirradiation period of a vitamin C-free diet is an essential factor in the success of roentgen therapy and that when the ascorbic acid level in the blood is reduced at the time of the initial exposure to about 0.05 mg./100 cc., much better results are achieved.

It is possible that the same factor was partially responsible for poor results with roentgen therapy in 4 cases of generalized carcinomatosis and a case of hepatoma of the liver. In all these cases, the patients were placed on a vitamin C-free diet three to five days before the initial exposure when the ascorbic acid concentrations of the blood were still as high as 0.1–0.2 mg./100 cc. In all these well advanced and moribund cases of carcinoma, the results of roentgen therapy were discouraging. There was certain temporary improvement in the con-

dition of the patients but without any alteration in the course of the disease.

Four cases of teratoma of the testis have been treated with roentgen irradiation supplemented with a vitamin C-free diet. In one case without apparent metastases, the results of roentgen therapy should be considered as very satisfactory. In this case, the diet was properly applied and for more than two years after the initial and only course of roentgen therapy, the patient remained free from any evidence of his disease.

In another case of teratoma of the testis with multiple metastases, the response to roentgen therapy was at first considered satisfactory with prompt disappearance of the irradiated masses, but subsequently the patient died from the generalized carcinoma. In this case, the diet was properly applied and the ascorbic acid level of blood at the initial exposure was close to zero: 0.01 mg./100 cc.

In 2 other cases of teratoma with multiple metastases, the roentgen therapy was applied as a palliative measure and the diet started only a few days before the initial exposure. Both patients died.

The general impressions from our clinical investigation on the effect of a vitamin C-free diet on the results of roentgen therapy may be formulated as follows:

The malignant diseases of the lymphatic system benefit mostly from this method if it is properly applied. The radioresistant tumors without metastases respond to this method much more satisfactorily than one would expect with this type of growth in the patients on an unrestricted diet. In generalized carcinomatosis or sarcomatosis where some metastases might escape the effect of roentgen irradiation, this method seems to be of little if any advantage, so far as our limited experience with this type of disease indicates.

DISCUSSION

The classic work of Jules Brachet and his associates[1] demonstrated that roentgen rays exert destructive effects upon desoxyribonucleic acid of cells and nuclei and reduce the viscosity of thymonucleohistone. This discovery explains roentgen radiation-induced breakage of the chromosomes in fast-growing malignant tissue. Recent investigations revealed that ascorbic acid is not only an important factor in the conversion of folic acid to citrovorum factor (Welsh *et al.*) but that it takes part in the formation of desoxyribonucleic acid (Gol'dshtein *et al.*). By depriving the organism and specifically malignant tissue of ascorbic acid, the formation of desoxyribonucleic acid is abated and the growth of malignant tissue slowed down. This fact might explain the beneficial effect of a vitamin C-free diet, which brings down the ascorbic acid level in the blood and malignant tissue close to zero in roentgen therapy. In the absence of ascorbic acid, the formation of desoxyribonucleic acid might be affected and thus favorable environmental conditions for roentgen-ray action are created. On the other hand, in the malignant diseases of the lymphatic system, the formation of citrovorum factor, an enhancing factor in multiplication of the lymphatic elements, is arrested in the absence of ascorbic acid. Thus, a vitamin C-free diet acts as a mild antifolic preparation—a fact which should be taken into consideration in roentgen therapy of this type of malignant disease. Since the patients can be kept on a vitamin C-free diet for a period of from four to six months without inducing any symptoms of scurvy, as was demonstrated in the present clinical investigation, it appears that this method deserves further and more extensive trials.

It is necessary, however, to point out that the recent discovery of C. G. King, that glucose is a precursor to ascorbic acid and apparently takes an important part in the formation of desoxyribonucleic acid,[10] suggests the expansion of this study by supplementing a vitamin C-free diet with an induced hypoglycemia in roentgen therapy. It is assumed that such a combined

therapy should cause a greater shock to malignant cells and thus enhance the destructive power of roentgen rays upon them. Clinical studies along these lines are under way and the results will be reported by us in the future.

SUMMARY

Liposarcoma of guinea pigs kept on a vitamin C-free diet grew very slowly when compared with liposarcoma of the animals receiving an adequate supply of ascorbic acid. At the end of a thirty-day period, the average tumor weight of the first group was 7.4 grams as against 26.5 gm. of the second group.

Crocker rat carcinoma, 18 mm. in diameter, was destroyed completely by 10,000 r contact radiation delivered in a single dose to the animals kept on a regular diet.

Crocker rat carcinoma, 18 mm. in diameter, was partially destroyed and the tumor growth retarded by application of 3,000 or 5,000 r contact radiation in a single dose to the animals kept on a regular diet. All animals, of both groups, died subsequently from cancer.

Crocker rat carcinoma, 18 mm. in diameter, was completely destroyed by application of 3,000 or 5,000 r contact radiation delivered in a single dose to the animals kept on a diet which brought down the ascorbic acid content of tumor tissue close to zero. All animals of both groups survived.

Twenty-six patients affected with various types of malignant disease were placed on a vitamin C-free diet for a period of from four to six months. They tolerated this regimen well and no symptoms of scurvy were observed. The roentgen therapy was initiated after the ascorbic acid concentration of blood was brought down to 0.02–0.01 mg/100 cc. of plasma, or after fifteen to eighteen days of dieting. The diet was continued during the whole course of radiation therapy and for two to three months following irradiation.

The malignant diseases of the lymphatic system and the radioresistant tumors without metastases responded satisfactorily to this treatment, while with generalized carcinomatosis and sarcomatosis, no alteration of the course of the disease was observed.

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A NEW IMPROVED TYPE OF COLPOSTAT

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IN A previous publication[1] (1952) a new type of colpostat was described for use in the treatment of cancer of the cervix uteri and other pelvic neoplasms. With this colpostat it is possible to place radium sources accurately in each lateral fornix under direct vision and to maintain constant position throughout the treatment. It is also possible with this instrument to take full advantage of the distensibility of the vaginal vault and obtain the maximum lateral spread of the radium sources for the individual patient.

Further experience with the colpostat has enabled us to make a number of useful improvements in its design. The colpostat is now made up of two component units, each unit consisting of an ovoid connected to one ring of a center locking device with a long handle. Both units are joined at this center locking device which functions as a pivot and has an adjustable tension mechanism. A hollow cylinder within each ovoid holds a single capsule or tube of radium. The ovoids are manipulated into position in the lateral vaginal fornices by means of the long handles pivoting through the center locking device. The distance between the centers of the ovoids, hence the radium sources, is measured with a calibrated arc.

The ovoids are made of nylon, all other parts are brass or steel. Nylon was chosen for the ovoids because of its hardness, lightness, strength, and durability. It is not altered by sterilization in an autoclave. It machines like steel. The transverse diameter of the ovoid is 2 centimeters. The rounded cap screws on and off easily and its tip is shaped hexagonally to fit a special wrench that is supplied. A hollow cylinder is bored in the middle of the long axis of the ovoid to a size just sufficient to hold the desired capsule of radium. If a short radium capsule is to be used in an ovoid made for a longer one, it can be fitted with a suitable adapter to maintain its position in the middle of the long axis.

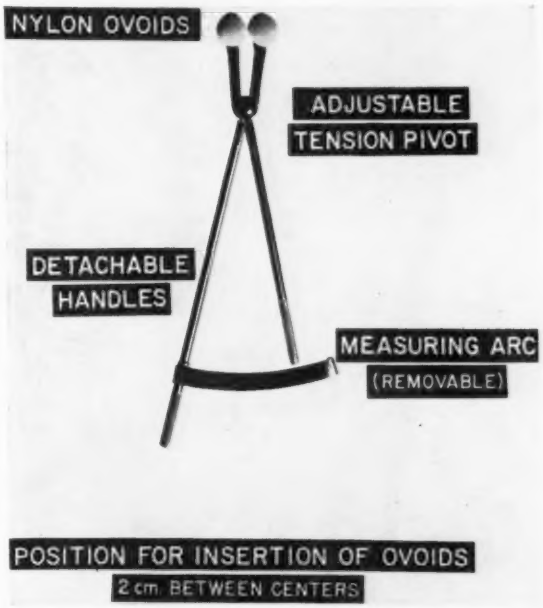

FIG. 1.

Each ovoid is held at its equator by a narrow brass supporting ring which is connected by a short rod to one of the rings of the center locking device. A small peg on the ovoid fits into a little notch on the supporting ring. The ovoid with its brass supporting ring is inclined at a 20 degree angle from the vertical in order to correspond somewhat with the usual angulation of the uterus on the axis of the vagina.

The center locking device is essentially an adjustable tension pivot. It consists of two separate rings, one above the other, held together with a slotted sleeve which is fixed to the lower ring and projects into the upper ring. A tapered screw fits into this slotted sleeve to wedge it firmly against the inner surface of the upper ring. The principle is similar to that of the braking mech-

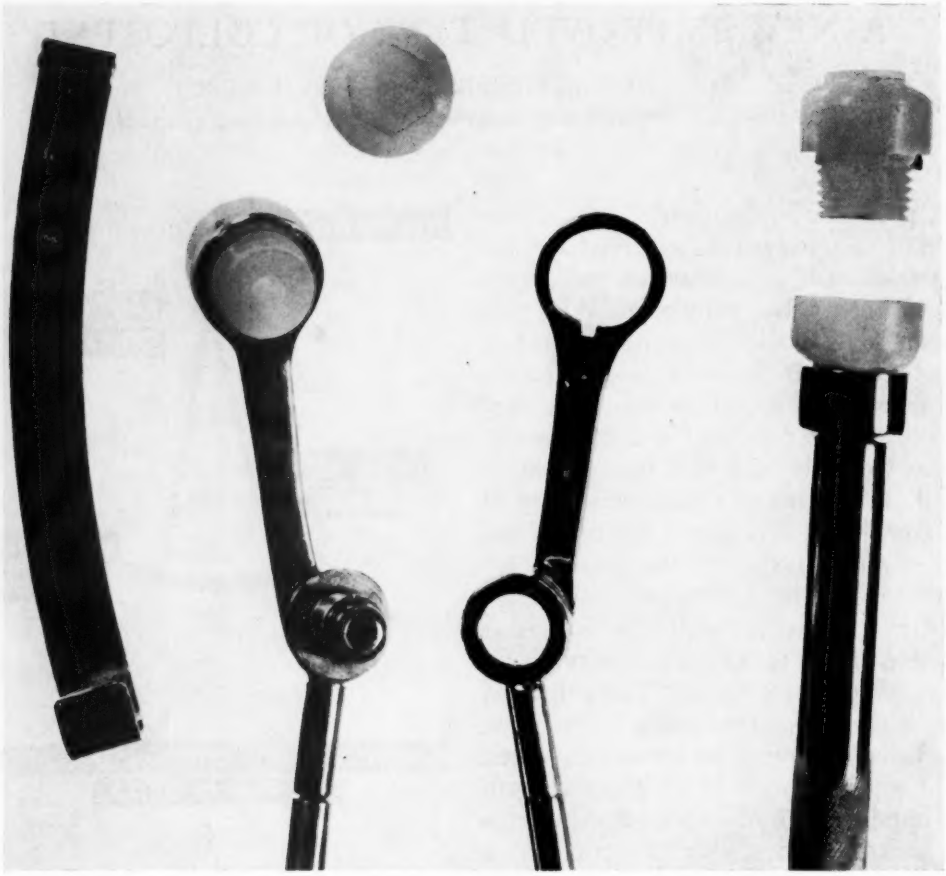

Fig. 2.

anism on the wheels of some motor cars. The degree of tension of this braking mechanism can be regulated by the tapered screw with a specially made Allen wrench. The proper degree of tension is that amount of friction which holds the ovoids in any desired position and at the same time permits their easy manipulation with the long handles attached to each ring of the center locking device.

In the unusual instance in which the introitus is too narrow to admit both ovoids together, the colpostat can be separated into its two component units and each ovoid then inserted individually. The units are re-joined by slipping the upper ring over the slotted sleeve. As a general rule, the vagina can be distended to accommodate both ovoids even if the introitus permits the insertion of only one at a time.

Approximating the handles separates the ovoids. The degree of separation is measured by a calibrated arc slipped on to the end of the longer handle. When the centers of the ovoids are 4 cm. apart, the handles come together. For further separation of the ovoids, the handles cross over each other. This arrangement allows the measuring arc to be a short one so that when it points to the right it measures 2 to 4 cm. separation and when reversed to the left, 4 to 6 cm. After the ovoids are placed in the lateral fornices and the degree of separation measured, a small amount of gauze packing is placed above and below the center locking device to maintain the colpostat in mid-position in the vagina. The handles are then removed. They need to be replaced only at the time of removal of the colpostat.

Dosage with varying degrees of separa-

Fig. 3.

tion of the ovoids was discussed in the previous article and will be the subject of a more detailed analysis in future publications.

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I wish to express my appreciation to Mr. Marcus Walter and Mr. Armando Cervi for their invaluable advice and technical assistance in improving the design of the colpostat.

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EDITORIALS

HYPOPHOSPHATASIA

IN 1948, Rathbun[1] described a new osseous developmental anomaly, characterized by abnormally low alkaline phosphatase activity, which he called "hypophosphatasia."

The case upon which Rathbun based his observations was that of a male infant who was first seen at the age of three weeks and was studied until the age of nine weeks when he died with tetanic convulsions. All bones (cartilaginous and membranous) showed roentgenologically a very low mineralization associated with grossly irregular cartilage maturation. The metaphyseal ends of the long bones exhibited trabecular projections of cartilage, extending into the diaphysis; the posterior arches of the lumbar vertebrae were indistinguishable from the soft tissue shadows; the ribs were deformed and showed flaring at the ends; and the calvarial bones were almost completely devoid of calcification. The alkaline phosphatase was absent in the blood serum and extremely low in the osseous tissue, kidneys and in the small intestine. Other interesting findings were slightly raised calcium and nonprotein nitrogen levels in the blood serum; first normal, then terminal increase of the phosphorus to a tetanic level in the blood serum; low excretion of calcium and phosphorus in the urine; postmortem demonstration of distention of the collecting tubules of the kidneys by hyaline and eosinophilic casts which did not contain calcium nor calcium phosphate; and finally, microscopic resemblance of the bone architecture to that of severe rickets containing abundant osteoid tissue.

Rathbun, after taking into consideration the possibility of osteogenesis imperfecta, achondroplasia and renal hyperparathyroidism in the differential diagnosis, arrived at the conclusion that his case did not fit into any of these entities. He believed that the primary failure in his case was a mesenchymal differentiation defect in that the osteoblasts are incapable of producing alkaline phosphatase. The absence of alkaline phosphatase would render the organism unable to free the organically bound phosphorus and this, in turn, would prevent overbalancing of the calcium-phosphorus ion solubility product which initiates calcification. Furthermore, the low alkaline phosphatase activity of the small intestine may have interfered with absorption of phosphorus. The low excretion of phosphorus in the urine, despite normal to high phosphorus levels in the blood serum, is attributed by Rathbun to the low tissue phosphatase of the kidneys. The terminal rise of the phosphorus to a tetanic level in the blood serum, which was probably started by transfusion of "banked blood," constitutes additional evidence of renal dysfunction, confirmed at autopsy by the finding of obstruction of the collecting tubules by casts. Rathbun does not believe, however, that the whole disease process is primarily of renal origin, since adequate renal function for other metabolites in his case was fully maintained during life. In fact, this observation was mainly the reason for his adoption of the name "hypophosphatasia" to "single out the remarkably low alkaline phosphatase levels" responsible for the defect.

In 1953, Sobel, Clark, Fox and Robinow[2]

[1] Rathbun, J. C. "Hypophosphatasia"—a new developmental anomaly. *A.M.A. Am. J. Dis. Child.*, 1948, *75*, 822–831.

[2] Sobel, Edna H., Clark, Leland C., Jr., Fox, R. Phyllis, and Robinow, Meinhard. Rickets, deficiency of "alkaline" phosphatase activity and premature loss of teeth in childhood. *Pediatrics*, April, 1953, *11*, 309–321; also, Sobel, Edna H., Clark, L. C., Jr., and Robinow, M. Report on disorder of skeleton resembling rickets, associated with loss of teeth and deficient alkaline phosphatase activity in 2-year-old child. *A.M.A. Am. J. Dis. Child.*, 1952, *83*, 410–412.

reported a case exhibiting similar features. A girl, one and one-half years of age, showed osseous disturbances and the loss of most of her deciduous teeth. Roentgenograms of the skeleton revealed poor mineralization with symmetric defects in the metaphyseal ends of the long bones at the sites of most rapid growth and bowing of the diaphyses. The sternal rib ends were flared and irregularly mineralized. Contrary to what was observed in Rathbun's case, however, the vertebrae and calvarial bones appeared normal. There was irregular calcification of deciduous and permanent teeth. The alkaline phosphatase was abnormally low in the blood serum and considerably reduced in the tissues of the liver and the costochondral junction as was shown by biopsy specimens. There were normal calcium and nonprotein nitrogen levels in the blood serum and there were no signs of renal dysfunction. The inorganic phosphate level in the blood serum was at the relatively high value considered normal for infancy. The microscopic appearance of the rib architecture was consistent with rickets.

This case was studied for a period of two years. Although various forms of treatment remain ineffective, the child continues to be in reasonably good health. Serial roentgenograms revealed that the skeletal disease is slowly progressing, deformities of the legs and thorax being the most obvious signs. There is, however, evidence of a distinct increase in the length of bones and she is gaining in height and weight at a satisfactory rate. She has lost most of her deciduous teeth. The alkaline phosphatase activity in the blood serum continues to remain very low and the inorganic phosphate level has not decreased as would be expected with increasing age.

Sobel, Clark, Fox and Robinow[2] also present partial data on 5 additional patients varying in age from two and one-half months to eight and one-half years, who had clinical and roentgenological signs of severe rickets and in all of whom a low alkaline phosphatase activity was demonstrated in the blood serum. Based on these observations they, too, favor the hypothesis that the growing bone requires the presence of alkaline phosphatase for normal calcification and that, therefore, the above described osseous defect, which most probably is genetically determined, may be related to a disturbance in the local factor.

Recently, Engfeldt and Zetterström[3] of Stockholm, Sweden, made an important contribution to the subject by studying in a similar case the properties of the organic and inorganic constituents of osseous tissue and its ultrastructure by biophysical methods. Their case was that of a five month old female infant who, when first seen, showed signs of a general skeletal disease resembling rickets and who had symptoms of a renal lesion. Roentgenograms of the skeleton revealed low mineralization generally. The metaphyses of all long bones showed marked fraying, fragmentation and deformation. Distinct changes were also present in the structure of the epiphyses. The ribs were considerably demineralized and there were several poorly healing fractures. There were large diastases between the different bones of the calvarium due to absence of mineralization. There was a normal number of bone centers. Roentgen study of the urinary system revealed reduced concentrating ability of the kidneys, but there was no evidence of renal calcification. The alkaline phosphatase activity in the blood serum was low and there was a slight rise in the serum calcium and nonprotein nitrogen levels. The serum phosphate level was, on the whole, normal for the patient's age.

The child was treated by various means but the disease continued to advance. The weight gain ceased altogether, the extremities became rather short in relation to the trunk and a sharp thoracolumbar kyphosis developed. At the age of ten months she died with symptoms of pulmonary and

[3] Engfeldt, B., and Zetterström, R. Osteodysmetamorphosis fetalis; a clinical-pathological study of a congenital skeletal disease with retarded growth, hypophosphatasemia and renal damage. *J. Pediat.*, Aug., 1954, *45*, 125–140.

cardiac failure. Postmortem examination revealed a generalized skeletal disease with marked inhibition of growth and greatly retarded calcification and a renal disease characterized by nephrocalcinosis with nephrocirrhosis. The alkaline phosphatase activity was very low in the bone tissue and depressed in the kidneys.

The biophysical methods carried out by Engfeldt and Zetterström included microradiography to determine the degree of mineralization and the distribution of mineral salts in different structures of the bone tissue; autoradiography to investigate the Ca^{45} uptake in vitro and thus gain some information as to the ion exchange of the mineral salts; roentgen-ray diffraction to study the ultrastructure of the bone; microphotography in transmitted and polarized light to examine the collagen pattern of the decalcified microradiographed bone; and, finally, microradiography with a lower voltage to analyze the deposition and distribution of the calcium salts in the kidneys.

Despite these exhaustive studies it has been impossible to establish any definite etiology for the disorder. Engfeldt and Zetterström state that the low alkaline phosphatase activity may be the primary cause or may be a secondary manifestation of a generally disturbed cellular function. There are strong indications that, in one way or another, the enzyme alkaline phosphatase is concerned with bone formation, thus supporting the views of Rathbun[1] and of Sobel, Clark, Fox and Robinow.[2] They suggest, however, that because of the characteristics of the osseous disturbances and since the condition is of fetal origin, the name of "osteodysmetamorphosis fetalis" be used for its designation.

At the last meeting of the American Roentgen Ray Society held in Washington, D. C., September 21 to 24, 1954, Neuhauser and Currarino[4] presented an excellent exhibit of a series of similar cases which they collected from various sources. The principal group comprised infants who were severely affected but also included were a few patients slightly more advanced in age with milder forms of the disease. Four patients with very severe abnormality of the skeleton who survived only briefly were included as probable examples of the extreme form of the disorder, although in these cases the diagnosis was presumptive since no chemical determinations were made. Neuhauser and Currarino,[4] like Rathbun,[1] use the term "hypophosphatasia" to emphasize the role of the abnormally low alkaline phosphatase activity of the blood serum and, in the patients who were studied, of the bones and other tissue as the underlying cause of the disorder.

Obviously, the very few cases reported so far do not, as yet, permit an accurate etiologic and pathogenetic evaluation of this new disorder. There can be no doubt, however, that clinically, roentgenologically and pathologically the entity is well delimited and that it may be classed in the group of genetically determined developmental anomalies of bone. It is also probable that, as shown by the unusual collection of cases exhibited by Neuhauser and Currarino, the condition occurs more frequently than is generally assumed.

T. Leucutia, M.D.

[4] Neuhauser, Edward B. D., and Currarino, Guido. Hypophosphatasia. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., Nov., 1954, *72*, 875.

THE FIFTH INTER-AMERICAN CONGRESS OF RADIOLOGY

THE Fifth Inter-American Congress of Radiology will hold its meeting at the Shoreham Hotel, Washington, D. C., on April 24–29, 1955, under the presidency of Dr. James T. Case.

The program which has been arranged for the Congress is a comprehensive one covering all phases of radiology. There are listed forty communications covering the field of radiodiagnosis, radiotherapy, radiophysics and radiobiology, and in addition to these communications there have been arranged three important symposia, one dealing with "Cancer of the Lung." This symposium will be moderated by Dr. Leo G. Rigler and, in addition to being moderator, Dr. Rigler himself will deliver an important paper on the "Natural History of Lung Carcinoma." This symposium includes such well known physicians as Dr. Alexander Gilliam of the United States Public Health Service, who will discuss the "Etiology of Lung Carcinoma"; an outstanding radiologist from Cordoba, Argentina, Dr. S. Di Rienzo, will discuss the "Present Knowledge of Methods in the Diagnosis of Lung Carcinoma," and a radiological colleague from Havana, Cuba, Dr. Laura Fariñas, will present a paper on "Methods of Roentgen Diagnosis in Lung Carcinoma." So one may readily see from this that the symposium on "Cancer of the Lung" promises to be one of the outstanding events of the Congress. A second symposium is to be given on "New Trends in Cancer" and a third symposium deals with "Radioactive Isotopes," with particular reference to newer applications in clinical cases as well as a review of accumulated experience with those radioisotopes used relatively more often in the past, such as radioactive iodine in thyroid diseases and radioactive gold.

In addition to the extensive communications covering various phases of radiodiagnosis, radiotherapy, radiophysics, and radiobiology and the three symposia, Refresher Courses will be given in English and Spanish by outstanding authorities in different fields of the specialty. Each of these Refresher Courses will last about one and a half hours.

In addition to the extensive scientific program, there has been arranged one of the largest Scientific Exhibits ever offered at a radiological congress. This Scientific Exhibit will include many of the newer contributions and accomplishments in radiology. Also, there has been organized a very outstanding Technical Exhibit in which the manufacturers will display their most recent developments in radiological equipment and discuss the technical aspects and importance of this new equipment.

On Saturday, April 30, one of the interesting sessions of the Congress will be held at the National Cancer Institute of the National Institutes of Health in Bethesda, Maryland.

The Fifth Inter-American Congress of Radiology follows immediately after the annual meeting of the American Radium Society which holds its sessions at the Shoreham Hotel from April 21 to April 23, 1955, so one may readily take advantage of two outstanding scientific meetings. The Preliminary Program of the American Radium Society appears elsewhere in this issue.

Membership in the Congress is open to all doctors of medicine specializing in radiology, radiophysics, and radiobiology, and the privilege of attending the meetings is open to all doctors of medicine.

In addition to the scientific program, a social program has been planned to permit of visits not only to medical institutions of scientific interest but to the many other cultural institutions and monuments of great importance in the City of Washington, and due to a rather fortuitous circum-

stance the Philadelphia Symphony Orchestra under the direction of the renowned and world-famous Eugene Ormandy will give a private concert in Constitution Hall on Wednesday evening, April 27. So the Fifth Inter-American Congress of Radiology promises to be outstanding in all respects and one can scarcely afford to miss such a rich opportunity.

For the benefit of all who are interested, application blanks for advanced registration are available from the office of the American College of Radiology, 20 North Wacker Drive, Chicago 6, Illinois.

It is with profound regret that we have learned of the death of Dr. Leon J. Menville of New Orleans. His death occurred on January 24, 1955. Dr. Menville was one of the outstanding radiologists of the world and was for a number of years Editor of *Radiology*, which stamps him as a man of the finest qualities. A more extended account of Dr. Menville's life will be published in one of the future numbers of the JOURNAL.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Palmer House, Chicago, Ill., Sept. 20–23, 1955.

American Radium Society
Secretary, Dr. R. E. Fricke, Mayo Clinic, Rochester, Minn. Annual meeting: Shoreham Hotel, Washington, D. C., April 21–23, 1955.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: 1955, to be announced.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois. Annual meeting: 1956, to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual Meeting, Atlantic City, N. J., June 6–10, 1955.

Fifth Inter-American Congress of Radiology
Secretary-General, Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa. Meets at Shoreham Hotel, Washington, D. C., April 24–29, 1955.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. J. A. Norton, 843 Donaghey Bldg., Little Rock, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Radiological Society
Secretary, Dr. Daniel G. Butera, 709 E. 39th St., Brooklyn, N. Y. Meets first Thursday of each month October through April.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

Buffalo Radiological Society
Secretary, Dr. Clayton G. Weig, 135 Linwood Ave., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse, N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. E. Burns Lewis, 670 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cleveland Radiological Society
Secretary, Dr. H. F. Inderlied, 11311 Shaker Blvd., Cleveland 4, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. S. A. Patterson, Larimer County Hospital, Fort Collins, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. B. B. Alicandri, 20 Maple St., Springfield, Mass. Meets second Friday October and April.

Dallas-Fort Worth Radiological Club
Secretary, Dr. O. H. Grunow, 650 Fifth Ave., Fort Worth, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. F. Lang, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, Oct. through May, at David Whitney House, 4421 Woodward Ave., at 6:30 P.M.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. J. T. Shelden, Box 1021, Lakeland, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Herbert M. Olnick, 417 Persons Bldg., Macon, Ga.

Greater Miami Radiological Society
Secretary, Dr. A. S. Capi, 300 N. 20th Ave., Hollywood, Fla. Meets monthly third Wednesday at 8 P.M. at various South Florida Hospitals.

Houston Radiological Society
Secretary, Dr. W. C. Owsley, 6409 Fannin, Houston 25, Texas. Meets fourth Monday each month at Texas Children's Hospital.

Idaho State Radiological Society
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. John A. Robb, 238 Hume-Mansur Bldg., Indianapolis 4. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society, The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. A. M. Cherner, Hays, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. David Shapiro, 323 East Chestnut St., Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Kings County Radiological Society
Secretary, Dr. Solomon Maranov, 1450 51st St., Brooklyn 19, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Oscar Harvey, 3741 Stocker St., Los Angeles 8, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

Maine Radiological Society
Secretary, Dr. W. A. Russell, Augusta General Hospital, Augusta, Maine. Meets in June, October, December and April.

Maryland Radiological Society
Secretary-Treasurer, Dr. Paul W. Roman, 1810 Eutaw Place, Baltimore 17, Maryland.

Memphis Roentgen Society
Secretary, Dr. B. E. Greenberg, 294 Annella St., Memphis 11, Tenn. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

Mid-Hudson Radiological Society
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

Milwaukee Roentgen Ray Society
Secretary, Dr. R. W. Byrne, 3321 N. Maryland Ave., Milwaukee 1, Wis. Meets monthly on fourth Monday at University Club.

Minnesota Radiological Society
Secrrtary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

Mississippi Radiological Society
Secretary, Dr. John W. Evans, 117 N. President St., Jackson, Miss. Meets third Thursday of each month at Hotel Edwards, Jackson, at 6:00 P.M.

Montana Radiological Society
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Meets at least once a year.

Nassau Radiological Society
Secretary, Dr. Alan E. Baum, Hicksville, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

Nebraska Radiological Society
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Oamaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets third Friday of each month, October through May, at Hotel Commander, Cambridge, Mass.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. Sidney Rubenfeld, 477 First Ave., New York 16, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. W. C. Sternbergh, Charlotte Memorial Hospital, Charlotte, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. Marianne Wallis, St. Joseph's Hospital, Minot, N. Dak. Meetings by announcement.

North Florida Radiological Society
Secretary, Dr. Ivan Isaacs, 1645 San Marco Blvd., Jacksonville, Florida. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. D. H. Baxter, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April.

Northern California Radiological Society
Secretary, Dr. H. B. Stewart, 2920 Capitol Ave., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

Ohio State Radiological Society
Secretary, Dr. M. M. Thompson, Jr., 319 Toledo Medical Bldg., Toledo 2, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. F. C. Shipps, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. J. R. Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Next annual meeting at Berkshire Hotel, Reading, Penna., May 20 and 21, 1955.

Philadelphia Roentgen Ray Society
Secretary, Dr. H. M. Stauffer, Temple University Hospital, Philadelphia 40, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets second Wednesday of month, October through June at Hotel Roosevelt.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Paul W. Roman, 1810 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

Radiological Section, Connecticut Medical Society
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of Greater Cincinnati
Secretary, Dr. Wm. R. Dickens, Cincinnati General Hospital, Cincinnati 29, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

Radiological Society of Hawaii
Secretary, Dr. H. C. Chang, 1282 Emma St., Honolulu 13, T. H. Meets third Monday evening of each month at designated hospitals.

Radiological Society of Greater Kansas City
Secretary, Dr. E. H. Stratemeier, Jr., 1010 Rialto Building, Kansas City 6, Mo. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. J. T. Brierre, 700 Audubon Bldg., New Orleans. Meets annually during Louisiana State Medical Society Meeting.

Radiological Society of New Jersey
Secretary, Dr. Carye-Belle Henle, 195 North 7th St., Newark, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

Radiological Society of Southern California
Secretary, Dr. George Jacobson, 1200 N. State St., Los Angeles 33, Calif.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital,

Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Henry H. Forsyth, Jr., 40 Meigs St., Rochester, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. John H. Freed, 4200 East Ninth St., Denver 7, Colo.

St. Louis Society of Radiologists
Secretary, Dr. W. B. Seaman, 510 South Kingshighway, St. Louis 10, Mo. Meets fourth Wednesday each month, except June, July, August and September.

San Antonio-Military Radiological Society
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas Meets Brooke Army Medical Center Officers Mess first Monday of each month.

San Diego Radiological Society
Secretary, Dr. C. W. Bruner, 2456 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. T. M. Fullenlove, 110 El Verano Way, San Francisco 27, Calif. Meets quarterly at Grison's Steak House.

Section on Radiology, California Medical Association
Secretary, Dr. H. R. Morris, 1027 "D" St., San Bernardino, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary, Dr. John A. Long, 1801 K St., N.W., Washington 6, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M. September to May inclusive.

South Bay Radiological Society
Secretary, Dr. H. R. Berman, 309 St. Claire Bldg., San Jose, Calif. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. William A. Klauber, Self Memorial Hospital, Greenwood, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. G. K. Henshall, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

Tri-State Radiological Society
Secretary, Dr. S. N. Tager, 219 Walnut St., Evansville, Ind. Meets last Wednesday of Oct., Jan., March and May, 8:00 P.M. at Elks' Club in Evansville.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Eva L. Gilbertson, 1317 Marion St., Seattle 4, Wash. Meets fourth Monday of each month from September through May at 610 Pine St., Seattle.

West Virginia Radiological Society
Secretary, Dr. W. Paul Elkin, 515 Medical Arts Bldg., Charleston, W. Va. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. M. G. Priestman, New Rochelle Hospital, New Rochelle, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. Wm. W. Saunders, Veterans Administration Hospital, San Francisco 21, Calif. Meets monthly, third Thursday at 7:45 P.M., Lane Hall, Stanford University Hospital.

Cuba, Mexico, Puerto Rico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexican de Radiología, A. C.
Secretary General, Dr. Eugenio Toussaint, Calle del Oro No. 15, Mexico 7, D.F. Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. Rafael A. Blanes, Ave. Ponce de Leon 1175, Santurce, P. R.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

Association of Radiologists of the Province of Quebec
Secretary, Dr. Jean-Louis Léger, 1560 Sherbrooke St., Montreal, Que. Meets four times a year.

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicales
General Secretary, Dr. Ls Ivan Vallée, 1058 rue St-Denis, Montreal 18, Canada. Meets third Saturday each month.

College of Radiologists (Australia and New Zealand)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro Sede, Córdoba
President, Prof. Dr. David L. Caro, Corro 86, Córdoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6° piso, Bogota, Colombia. Meets last Thursday of each month.

Sociedad Peruana de Radiologia
Secretary General, Dr. Amador Holgado V. Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Société Française d'Electro-Radiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX°, France.

Ceskoslovensk společnost pro rëntgenologii a Radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgen-Gesellschaft
Secretary, Dr. med. Peter Kröker, Evangelisches Krankenhaus, Huyssens Stiftung, (22a) Essen.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

Nederlandse Vereniging voor Electrologie en Roentgenologie
Secretary, Dr. B. J. Rethmeier, Bornsestraat 378, Almelo, Netherlands.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw Poland.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

Wroclaw Section, Polish Society of Radiology
Secretary, Dr. R. Marciniak, Akad. Medyczna Wroclaw, 68 Curie-Sklodowska St., Wroclaw, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wroclaw.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S.I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société-Suisse de Radiologie)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

India

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

In the future, the list of Meetings of Radiological Societies will appear in every other issue of the Journal, that is, in 1955, in May, July, September and November.

AMERICAN RADIUM SOCIETY
PRELIMINARY PROGRAM

The following is the tentative program which has been arranged by the Program Committee under the chairmanship of the President, Dr. John E. Wirth, for the Thirty-seventh Annual Meeting of the American Radium Society to be held at the Shoreham Hotel, Washington, D. C., Thursday, Friday and Saturday, April 21, 22 and 23, 1955.

Attention is called to Dr. Wirth's editorial comment on the meeting which appeared in the February, 1955, issue of the JOURNAL, page 310, and to the fact that the Fifth American Congress of Radiology is to be held at The Shoreham on April 24 to 29, which is immediately following the meeting of the American Radium Society. It is again emphasized that reservations be made promptly through Mr. L. Gardner Moore, Shoreham Hotel, Washington 8, D. C.

Thursday, April 21, 1955
Registration: 9:00 A.M.–12:00 M.
Foyer, West Ballroom

Opening Session: 2:00–5:00 P.M.
West Ballroom

Convening of the Thirty-seventh Annual Meeting
Address of Welcome
Presidential Address. John E. Wirth, M.D., Pasadena, Calif.
Symposium: Endometrial Cancer. Franklin L. Payne, Philadelphia, Pa., Moderator.
This will be a panel discussion on the advisability or advantages of preoperative irradiation. Two persons will take the affirmative while two others will support the contrary view.
Executive Session

Evening Session: 7:00–9:30 P.M.

Informal Dinner (Wives and Guests Welcome)
The Janeway Lecture (Wives and Guests Welcome)
Title and Lecturer to be announced.

Friday, April 22, 1955
Morning Session: 9:00 A.M.–12:00 M.

Executive Session
Scientific Session: Norman A. McCormick, M.D., Ontario, Canada, Chairman.
Radiation Therapy of Carcinoma of the Urinary Bladder. Ira H. Lockwood, M.D., and Samuel B. Chapman, M.D., Kansas City, Mo.
Point Source Intracavitary Irradiation for Carcinoma of the Bladder. Milton Friedman, M.D., New York, N. Y., and Lloyd G. Lewis, M.D., Washington, D. C.
Treatment of Malignant Effusions by Intracavitary Injection of Radioactive Gold Colloid. Chu H. Chang, M.D., New Haven, Conn.
Observations on Growth Rates of Human Tumors. Vincent P. Collins, M.D., R. Kenneth Loeffler, M.D., and Harold Tivey, M.D., Houston, Texas.
Time-Dose Relationships. Lucile A. Du Sault, Detroit, Mich. Discussion by Edith H. Quimby, Sc.D.
Luncheon

Afternoon Session: 2:00–5:00 P.M.

Scientific Session: W. Edward Chamberlain, M.D., Philadelphia, Pa., Chairman.
The Management of Cancer of the Base of the Tongue. John V. Blady, M.D., and Theodore A. David, M.D., Philadelphia, Pa.
An Attempt to Correlate Radiation Dose with the Incidence of Cataracts in Patients. George R. Merriam, Jr., M.D., and Elizabeth F. Focht, B.A., New York, N. Y.
The Future of Radiotherapy and Radiobiologic Research. Henry S. Kaplan, M.D., Bethesda, Md.
Portable Isotopic X-Ray Units. A. T. Krebs, Ph.D., Fort Knox, Ky.
A Comparator Chamber from Commercially Available Components. E. Dale Trout, D.Sc., and John P. Kelly, B.S., Milwaukee, Wis.
Executive Session

Annual Banquet

Cocktails, Foyer, Terrace Room
Annual Banquet, Terrace Banquet Room

Saturday, April 23, 1955
Morning Session: 8:30 A.M.–12:00 M.

Executive Session
Scientific Session: Grant H. Beckstrand, M.D.,

Long Beach, Calif., Chairman.

Symposium: Clinical Diagnosis and Pathological Aspects of Various Benign Lesions of the Breast and Their Relationship to the Development of Carcinoma of the Breast. The Clinical Diagnosis of Carcinoma of the Breast. Cushman D. Haagensen, M.D., New York, N. Y., Moderator.

Panel Discussion by clinicians, pathologist W. Purdy Stout, M.D., radiologists and an endocrinologist.

SECOND ROSS GOLDEN LECTURE

Dr. Eugene P. Pendergrass will deliver the second Ross Golden Lecture before the New York Roentgen Society on Monday, March 21, 1955, at the New York Academy of Medicine at 8:30 P.M. His topic will be "Some Considerations Concerning the Roentgen Diagnosis of Silicosis and the Responsibility of the Radiologist."

JOSEPH FREEDMAN LECTURES

On Saturday and Sunday, May 7 and 8, 1955, Dr. Felix G. Fleischner, Associate Clinical Professor of Radiology, Harvard Medical School, and Director, Department of Radiology, Beth Israel Hospital, Boston, will deliver the seventh annual Joseph Freedman Lectures in Diagnostic Roentgenology at the University of Cincinnati College of Medicine, Cincinnati, Ohio. Radiologists desiring to attend are requested to write Dr. Benjamin Felson, X-ray Department, Cincinnati General Hospital, Cincinnati 29, Ohio, for further details.

PRIZE ESSAY IN THE HISTORY OF MEDICINE

Henry and Ida Schuman of New York take pleasure in announcing an annual award of $250 for an original prize essay in the history of medicine. The donors point out that the term "history of medicine" should not be too narrowly considered, *i.e.*, that the essays might range from fresh interpretations of the classical medical writers and their contributions (revealing the origin and growth of medicine and other sciences such as chemistry and physics) to social ideas in medicine and/or the relations between medicine and literature.

Medical students and interns in any American or Canadian institution are eligible for the award.

Papers should run approximately 5,000 words in length and should be submitted by April 1 of each year to the *Journal of the History of Medicine* whose editorial board will pass on the suitability of the winning essay for publication in that journal at an early date.

BROOKLYN RADIOLOGICAL SOCIETY

The Brooklyn Radiological Society has recently been organized. Its temporary officers are as follows: *President*, Dr. Emmanuel Mendelson, Brooklyn, N. Y., *Vice-President*, Dr. John Pepe, Brooklyn, N. Y., *Secretary-Treasurer*, Dr. Daniel G. Butera, 709 E. 39th Street, Brooklyn, N. Y. Meetings are held the first Thursday of each month from October to April, inclusive.

GREATER MIAMI RADIOLOGICAL SOCIETY

The following new officers were elected at the meeting of the Greater Miami Radiological Society held on January 19, 1955, in Miami, Florida: *President*, Dr. David Kirsch, Miami, Florida; *Vice President*, Dr. Albert McCallen, Coral Gables, Florida; *Secretary-Treasurer*, Dr. Andre S. Capi, 300 N. 20th Avenue, Hollywood, Florida. The Society will continue to have its monthly meetings on the third Wednesday at 8:00 P.M., at various South Florida Hospitals.

HOUSTON RADIOLOGICAL SOCIETY

At the November, 1954, meeting of the Houston Radiological Society, the following officers were elected for the ensuing year: *President*, Dr. Harry Fishbein; *Vice-President*, Dr. Frank Windrow; *Treasurer*, Dr. Roland Carroll; *Secretary*, Dr. W. C. Owsley, 6409 Fannin, Houston 25, Texas. The Society meets the fourth Monday of the month at the Texas Children's Hospital.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return or the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Clinical Roentgenology. Volume I. Developmental and Systemic Conditions and Local Lesions in the Extremities. By Alfred A. de Lorimier, M.D., Radiologist, Saint Francis Memorial Hospital, San Francisco, California; Henry G. Moehring, M.D., Radiologist, Duluth Clinic, Duluth, Minnesota; John R. Hannan, M.D., Radiologist, Lake County Memorial Hospital, Painesville, Ohio. Cloth. Price, $18.50. Pp. 495, with 782 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1953.

Clinical Roentgenology. Volume II. The Head, Neck and Spinal Column. By Alfred A. de Lorimier, M.D., Radiologist, Saint Francis Memorial Hospital, San Francisco, California; Henry G. Moehring, M.D., Radiologist, Duluth Clinic, Duluth, Minnesota; John R. Hannan, M.D., Radiologist, Lake County Memorial Hospital, Painesville, Ohio. Cloth. Price, $18.50. Pp. 488, with 734 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1954.

The first two volumes of this new textbook of roentgen diagnosis deal with the skeletal system. Each of the conditions discussed is assigned an independent chapter, and each chapter deals with the basic pathologic process, roentgen signs, clinical manifestations, laboratory findings and differential diagnosis. Well chosen roentgenograms with very good legends illustrate the characters of the various lesions. A brief list of important bibliographic references terminates each chapter.

The authors have adhered to this overall plan consistently, using a minimum of words to point out diagnostic criteria, pitfalls, and limitations of the method, thus making their presentation coherent and eminently readable. Some of their views are debatable; for instance, they regard sarcoid as a tuberculous osteomyelitis, Paget's disease as an endocrine disorder, and bursitis—as distinct from peritendinitis—as an infection akin to cellulitis. Some of the developmental disturbances are not listed, *e.g.*, diastematomyelia and Marfan's syndrome. The description of the reticuloses, the thyroid dysfunctions and the blood dyscrasias is not complete. These are flaws which could easily be corrected. What is outstanding is the general design or master plan of the text.

The two volumes are handsomely printed and attractive. The illustrations are among the best to be found in American publications. The authors and publisher deserve credit for giving us a refreshingly concise new treatise. Systematic without being tiresome, these first two volumes make the pertinent facts and findings readily available, particularly to the graduate student. It is perhaps inevitable that in a book which aims mainly at clarity and brevity, a few somewhat arbitrary opinions appear here and there and that completeness is not a primary object. But the work is unusually well organized. As it matures with future editions, it may eventually become a standard American text of diagnostic roentgenology.

Albert Oppenheimer, M.D.

I nuovi mezzi d'indagine nello studio radiologico del mediastino-stratigrafia. By Pietro Amisano. Vol. I: 2ª Relazione, ATTI del XVII Congresso Nazionale di Radiologia Medica. Paper. Pp. 106, with 79 illustrations. Instituto per la Diffusione di Opere Scientifiche, Milano, 1952.

This work is essentially a study of the newer forms of stratigraphy (laminagraphy) as they are applied to mediastinal diagnosis. The first half of the book is devoted to the general theory of laminagraphy and to its practical applications. Considerable space is devoted to axial transverse laminagraphy according to the technique of Vallebona.

Normal mediastinal laminagrams of children and adults are presented and discussed. This is followed by a description of the laminagraphic appearance of thymic hypertrophy, paravertebral calcifications, glandular tumors, neuromas, pneumonectomies, fibrothorax, aortic aneurysms and congenital heart disease. A chapter is devoted to the technique of gas insufflation of the mediastinum. This monograph is interesting because of the high quality of the roentgeno-

grams shown and because of the reliance which the author places on the laminagraphic method.

Cesare Gianturco, M.D.

Radiologie du Rein et de l'Uretère. Par R. Gouverneur, Chirurgien de l'Hôpital Necker, Chef du service d'Urologie, P. Porcher, Radiologiste de l'Hôpital Saint-Antoine, and R. Hickel, Radiologiste du service d'Urologie de l'Hôpital Necker. Paper. Price, 5.400 fr. Pp. 440, with 412 illustrations. Masson et Cie, Editeurs, 120, Boulevard Saint-Germain, Paris (VI^e), France, 1953.

This beautifully printed work covers the anomalies and diseases of the kidneys and ureters. It is safe to declare that no renal or ureteral affection can be adequately studied without the aid of simple roentgenography or roentgenography after intravenous injection of some substance which by its elimination evaluates renal function and visualizes the characteristics of form, and the volume of the calyces, the renal pelves and the ureters. The authors use the commonly employed European terminology which speaks of the intravenous examination as urography and retrograde study with opaque materials as pyelography. Pyelography has lost many of its indications because of the fact that urography generally gives sufficient information; pyelography is now generally reserved for those cases where it will afford a better demonstration of a lesion which is not shown well enough with urography.

The text presents the fruit of thirteen years of teamwork, richly illustrated with excellent roentgenograms and explanatory drawings. The authors maintain the value of early compression of the ureters in doing excretory urography. They have found that early compression permits recognition of many lesions which are often overlooked when the compression is made late in the examination (renal tuberculosis misinterpreted as pyelonephritis or lithiasis, early malignant tumors) and have been able to avoid nephrectomies which would have been done on healthy kidneys. The authors believe that close collaboration between the urologist and the radiologist is of the highest value, and that it is unwise for the clinician to put too much restraint upon the radiologist or try to tell him too precisely what he should do or how he should do it.

James T. Case, M.D.

Cancer, Problemas Clinco-Terapeuticos. By Manuel Riveros, M.D., Professor of Surgical Clinics, School of Medicine of Asuncion, Paraguay, with the collaboration of twenty other authors. Cloth. Pp. 534, with 535 illustrations. Paz Montalvo, Madrid, Spain, 1953.

This book is an excellent example of the progressiveness and underlying strength of present-day Latin American medicine. The volume covers a variety of subjects, considered as problems of diagnosis or treatment of cancer: roentgenologic examination of maxillary tumors, of carcinoma of the bronchus, of retroperitoneal tumors, surgery of parotid tumors, of carcinoma of the esophagus; radiotherapy of Hodgkin's disease.

Dr. Riveros writes or contributes to chapters on adamantinomas, tumors of the small intestine, sarcomas of the breast, melanomas, glomus tumors and carcinoma of the prostate. Among the distinguished contributors to this volume one finds the well known names of Codas-Thompson, Roux-Berger, Di Rienzo, Frangella, Redon, Viacava and Pack.

Many of the chapters are concise, didactic and informative, but others waste space by lengthy narration of irrelevant data. The roentgenograms, reproduced in the positive, fail often to demonstrate details; the photomicrographs are rather poor and often worthless. Some of the clinical photographs illustrate very advanced cases which demonstrate little and may not encourage much the general practitioner for whom the book is intended. The reproduction of color photographs is excellent. Most chapters end with a well chosen list of references.

This book cannot fail in its aim of bringing to Spanish speaking physicians a wealth of information on the modern trends of cancer treatment and should result in a greater cooperation towards earlier diagnosis and treatment.

J. A. del Regato, M.D.

Teratomas. Atlas of Tumor Pathology, Section III—Fascicle 9. By Rupert A. Willis, D.Sc., M.D., F.R.C.P., Professor of Pathology, University of Leeds Medical School, Leeds, England, etc. Paper. Price, 50 cents. Pp. 58, with 45 illustrations. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1951. For sale by the American Regis-

try of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

Tumors of the Parathyroid Glands. Atlas of Tumor Pathology, Section IV—Fascicle 15. By Benjamin Castleman, M.D., Acting Chief, Department of Pathology and Bacteriology, Massachusetts General Hospital, and Assistant Professor of Pathology, Harvard Medical School. Paper. Price, 65 cents. Pp. 74, with 53 illustrations. Published by the Armed Forces Institute of Pathology, under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1952. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

Tumors of the Carotid Body and Related Structures (Chemoreceptor System). Atlas of Tumor Pathology, Section IV—Fascicle 16. By Philip M. LeCompte, M.D., Pathologist, Faulkner Hospital, Boston, Massachusetts, Instructor in Pathology, Harvard Medical School, Boston, Massachusetts. Paper. Price, 45 cents. Pp. 40, with 23 illustrations. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1951. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington, 25, D. C.

Tumors of the Lower Respiratory Tract. Atlas of Tumor Pathology, Section V—Fascicle 17. By Averill A. Liebow, M.D., Professor of Pathology, Yale University School of Medicine. Paper. Price, $1.25. Pp. 189, with 249 illustrations. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1952. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

Tumors of the Central Nervous System. Atlas of Tumor Pathology, Section X—Fascicles 35 and 37. By James W. Kernohan, M.D., Section on Pathologic Anatomy, Mayo Clinic, Rochester, Minnesota; Professor of Pathology, Graduate School, University of Minnesota; and George P. Sayre, M.D., Section on Pathologic Anatomy, Mayo Clinic, Rochester, Minnesota, Instructor in Pathology, Graduate School, University of Minnesota. Paper. Price, 90 cents. Pp. 129, with 126 illustrations. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1952. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

These inexpensive, unbound volumes form a part of a large series published by the Armed Forces Institute of Pathology. The entire series is an extensive atlas of tumor pathology, with individual volumes limited to specific organs or otherwise related structures.

The striking feature of these volumes is their beautiful illustrations. There are photographs of microscopic preparations with varying degrees of magnification and of gross specimens. They are reproduced on highly glazed paper with particularly fine cuts.

The text is rather limited. There are general remarks concerning the classification of the tumors described, the general symptomatology of the lesions, and the origin and natural history of the tumors. There are detailed descriptions of both the gross and microscopic pathological characteristics which are so beautifully illustrated in each instance. Of considerable interest is an extensive list of synonyms for each type of tumor. There are excellent bibliographic sections, and indeed, some of the illustrations are from previous published material. The atlas covers benign and malignant tumors.

Roentgenograms are occasionally reproduced as in discussion of parathyroid tumors or pulmonary tumors, but emphasis is on the viewpoint of the gross and microscopic pathology.

These volumes should be a part of any complete pathology library. It is interesting that material of this type can be published at so low a cost to the purchaser. Selected volumes, such as that dealing with tumors of the lower respiratory tract, would be of considerable interest to the radiologist.

E. F. Lang, M.D.

Stress Incontinence in the Female. By John C. Ullery, M.D., F.A.C.S., F.I.C.S., Obstetrician and Gynecologist, Pennsylvania

Hospital; Assistant Professor in Obstetrics and Gynecology, Jefferson Medical College; Associate in Gynecology and Obstetrics, Graduate School, University of Pennsylvania; etc. Cloth. Price, $6.75. Pp. 149, with 82 illustrations. Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, New York 1953.

Despite the earnest efforts of gynecologists, anatomists and physiologists for many years, stress incontinence of urine in the female continues to be a baffling and poorly understood clinical problem. In this lucid yet compact volume the author makes it clear why the results of treatments, nonsurgical and surgical, have not been uniformly satisfactory and what approaches must be utilized by clinicans if more consistent success is to be achieved.

A review of the embryology and anatomy of the urinary tract and its normal physiology and the complex factors which lead to abnormal structure and function of these organs shows at once that no routine method of treatment can ever be uniformly successful. Each case must be studied individually and intensively before an appropriate method of treatment can be selected. To make the proper evaluation the gynecologist must call upon the urologist, and particularly the radiologist for help.

Readers of these pages will be impressed by the author's emphasis upon the need for roentgenologic confirmation in determining the basic functional and anatomic derangements which must be corrected. He describes in detail the roentgenologic techniques which have been devised (cystography, urethography and cystourethrography) to portray the dynamic events of micturition and the specific lesions of stress incontinence. Excellent illustrations accompany this portion of the text. The chapter dealing with definitive treatment gives an excellent compilation of surgical techniques, amply illustrated, which the gynecologist may then elect once he has made a painstaking appraisal. In the final chapter evaluating the results of present day operative procedures, the author concludes that despite encouraging improvements in diagnosis and definitive treatment "much more work needs to be done before all the problems of stress incontinence are solved."

In his Foreword to this monograph, the British gynecologist Charles D. Read, who has himself contributed so extensively to our knowledge of stress incontinence, warmly commends this "critical review of virtually the whole of the literature on the subject." In the 143 pages of text, exclusive of bibliography and index, the author has given the results of much honest and worthwhile endeavor.

Harold C. Mack, M.D.

The Physics of Radiation Therapy. By Harold Elford Johns, M.A., Ph.D., F.R.S.C., Professor of Physics, University of Saskatchewan; Physicist, Saskatchewan Cancer Commission, Saskatoon, Saskatchewan, Canada. Cloth. Price, $8.50. Pp. 286, with illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1953.

As stated by the author, this book is an expansion of a set of notes which was printed privately and in limited number by the Saskatchewan Cancer Commission. It consists of 230 pages of text divided in 12 chapters, of two appendices and two indices.

The text is developed in orderly and logical sequence; in the first three chapters on basic physics, the reader is taken through the structure of matter and radiation, the production and properties of roentgen rays and the absorption of roentgen rays by matter.

The fourth chapter, entitled "Measurement of quantity of radiation," deals with the roentgen and its experimental realization by means of the standard ionization chamber and contains, moreover, practical information on the calibration of roentgen-ray machines with ionization chambers commercially available. The chapter on quality of roentgen rays covers the concept of half-value layer, equivalent wavelength and kilovoltage and discusses the variation of quality within a scattering medium.

The next two chapters concern themselves with the interaction of roentgen rays in phantoms. The subject of backscatter, depth dose and isodose are discussed in detail and bring to the reader a wealth of data scattered throughout the radiological literature. The practicing radiotherapist will find herein specific examples of isodose curve plotting relating to treatment of cancer of the larynx and of the esophagus. Appendix A supplements this chapter with isodose and depth dose information. The eighth chapter discusses the relation between energy absorption and the roentgen; in addition, the

concept of integral dose and the role of the tissue atomic number are considered with considerable clarity and didactic skill.

The next two chapters are devoted to radium and its active deposits and to radium dosage. Discussion of the latter follows the Manchester system in considerable detail with the aid of extensive charts taken from Meredith's book, *Radium Dosage*. The practicing therapist and the student will derive great help and benefit from the various examples quoted therein.

The chapter on high energy devices is concisely descriptive in character. In it, the basic principles of operation of the cyclotron, the betatron, the synchrotron, the nuclear reactor, the Van de Graaff generator, the resonant transformer and Co^{60} telecurie unit are described and references to monographs on protection are given.

The last chapter, "Artificial radioactivity," surveys nuclear transmutations and radioactive isotopes; since in fifteen pages only the salient points can be treated, this chapter cannot be considered a source of sufficient information for workers wishing to embark on isotope therapy or tracer work.

Some general observations are in order: Bibliographic annotations are supplied at the end of all chapters but, unfortunately, the very useful summaries are in evidence only for some. The literature covered is predominantly British and does not extend beyond 1950. Several typographical errors were discovered, of which the most unfortunate is in the first line of page 149, leading to an erroneous statement.

This volume is written specifically for the practicing radiotherapist, and as such it fulfills its mission to a considerable degree, although contact roentgen therapy is hardly mentioned and dose data are confined mainly to 200 and 400 kv. roentgen-ray machines. The style is crystalline and attractive and will undoubtedly win many friends. The publishers are to be congratulated on a fine printed product.

L. D. Marinelli

Nuclear Moments. By Norman F. Ramsey, Professor of Physics, Harvard University. Cloth. Price, $5.00. Pp. 169, with 38 illustrations. John Wiley & Sons, Inc., 440 Fourth Avenue, New York 16, New York, 1953.

The first four sections of this book consist of the author's chapter entitled "Nuclear Moments and Statistics" in Volume I of "Experimental Nuclear Physics," edited by E. Segrè, already reviewed in this Journal (January, 1955).

To that section, which dealt with those aspects of the subject concerned with nuclear physics, the author has added in this volume a fifth section dealing with topics of significance to the chemist and solid state physicist. In his addition of nearly fifty pages, he has maintained throughout the excellent qualities that characterized his first contribution.

L. D. Marinelli

Experimental Nuclear Physics. Volume II. E. Segrè, Editor. Cloth. Price $12.00. Pp. 600, with 73 illustrations and 37 tables. John Wiley & Sons, Inc., 440 Fourth Avenue, New York 16, New York, 1953.

The second volume of this series maintains the eminent quality and purpose of the first volume, namely to inform the reader about the main results obtained in nuclear physics up to the end of 1952.

The first section of this volume—and sixth of the series—is entitled "Survey of Nuclear Reactions" by Philip Morrison. It consists of 207 pages including two appendices and a profuse bibliography. The author, starting with the conservation laws of energy and momenta and a concise survey of nuclear reactions, leads the reader skillfully to the nuclear model, to the concept of nuclear level widths and to the several classifications of nuclear reactions, utilizing the concept of the compound nucleus. From the sixth chapter on, the treatise takes up theoretical discussions pertaining to particular reactions and their products. The last two chapters deal with nuclear fission and with reactions at very high energy.

The author concludes with a clear warning on the limitations of the treatment given to a subject undergoing active exploration and development. Despite the inherently difficult theoretical character of this chapter, the author has succeeded in providing an account of unusual clarity. The reviewer would have liked, however, an introductory chapter (or an appendix) on quantum theory cogent to the discussion, as a handy refresher for readers who have not cultivated the subject since their graduate school years.

The second part of the volume is entitled

"The Neutron" by Bernard T. Feld. It consists of five sections covering almost four hundred pages of dedicated effort.

Historical considerations, intrinsic properties and fundamental (n, p), (n, n) and (n, e) interactions are described in section 1 while interactions with nuclei are treated in section 2. Sources, detectors and neutron spectroscopy, including calibration of neutron sources are the subject matter in section 3. The fourth section covers the diffusion and slowing down of neutrons and includes the nuclear chain reaction. The fifth and last section covers the neutron diffraction, polarization and magnetic scattering.

This chapter is perhaps the most complete treatise available in English on the subject and has been written with highly commendable didactic skill. Prized on equal terms with the interesting style of presentation is the presence of an introduction in each section.

In conclusion, Volume II is an indispensable companion of Volume I in a series of texts of genuine intrinsic worth to students and research workers in this rapidly expanding field.

L. D. Marinelli

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Huang, Yun Shang, and Araki, Chisato. Angiographic confirmation of lateral ventricle meningiomas; a report of five cases. *J. Neurosurg.*, July, 1954, *11*, 337–352.

An accurate diagnosis of meningioma of the lateral ventricle by any of the conventional methods except angiography is very difficult and usually impossible. The authors present 5 cases in which a positive diagnosis of meningioma of the lateral ventricle was established. Four of these were diagnosed by angiography and in retrospect the other probably could have been diagnosed.

The angiogram will show elevation and straightening of the anterior cerebral artery due to dilatation of the ventricle and when the temporal horn is involved the middle cerebral group will be elevated. There is usually a maze of fine tortuous vessels in the region of the tumor in the arterial phase. The anterior choroidal artery is large and frequently tortuous because the major blood supply is from this vessel through the choroid plexus.

The venous phase will show a homogeneous increase in density in the tumor (the so-called venous stain). When the above findings are present a diagnosis of meningioma is indicated. Ventriculography will suggest the presence of a tumor but no clue as to cell type will be obtained with any procedure except angiography.—*Frank M. Windrow, M.D.*

Schlosshauer, B., and Möckel, G. Kontrastmittelübertritt ins Blut bei röntgenologischer Darstellung der Kieferhöhlen. (Passage of contrast material into the blood during roentgen examination of the maxillary sinuses.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, June, 1954, *80*, 708–713.

When pyridine-iodine compounds (as perabrodil, uroselectan B, etc.) are used as water-soluble contrast media, for the demonstration of pathology in the antrum, a certain amount is absorbed into the blood stream.

In 21 cases, the blood level of pyridine-iodine was determined. The blood level was found to be 0.2 mg. per cent in four hours, when the mucosa of the antra was normal. When inflammatory processes or polyps were present, the blood level was higher, up to a maximum of 1.39 mg. per cent. When compared with the blood level after intravenous pyelography, which is about 200 mg. per cent, this amount of the contrast medium in the blood is minimal. According to other authors, the blood level of this iodine compound is maximally 23.9 mg. per cent after retrograde pyelography, 29 mg. per cent in bronchography, and 2.6 mg. per cent in cystography. The maximum blood concentration of the chemical in the blood following contrast examination of the antra, is considerably lower than after these generally accepted procedures (1.3 mg. per cent). Allergic reactions, of course, are possible even after small amounts. The authors, however, did not see any severe allergic reaction in 116 contrast examinations of the maxillary sinuses. Routine testing for allergic phenomena, therefore, does not seem necessary and only the history of allergic reactions should be an indication for testing the reaction of the patient to the chemical.—*Hans W. Hefke, M.D.*

Browne, Kenneth M., and Stern, W. Eugene. Experimental observations concerning cerebral angiography. *A.M.A. Arch. Neurol. & Psychiat.*, April, 1954, *71*, 477–487.

The authors report their observations on 220 cerebral angiographic studies performed on 14 cats. They used a vertex-base roentgenographic projection to demonstrate the entire circle of Willis with its main branches as well as much of the extracranial carotid system. Ten per cent thorotrast or 35 per cent diodrast was injected by a compressed air system having a control valve so that injection pressures were controlled and reproducible. Photomicrographs were utilized to study the pial arteries.

Severe arterial constriction occurred frequently in the extracranial portions of the carotid artery during angiographic studies. Focal areas of spasm in the extracarotid arteries were noted following intravenous or intracarotid histamine or epinephrine. Neither of these changes was observed in the intracranial arteries.

Tortuosity of the basilar artery was increased with high systemic blood pressure and reduced when the animal was in shock.

Asymmetry in the lateral halves of the circle of Willis occurred following unilateral electrical stimulation of a cervical sympathetic trunk. This change did not occur in other angiograms and the authors concluded that there was no reflex stimulation of the cervical sympathetic trunk as a result of either manipulation or injection of the carotid artery.

In all but one case, microscopic observations of the pial arteries during carotid angiography revealed transient dilatation of these vessels following carotid injection of 70 or 35 per cent diodrast.—*D. V. Campbell, M.D.*

Neck and Chest

Newell, R. R., Chamberlain, W. Edward, and Rigler, Leo. Descriptive classification of pulmonary shadows; a revelation of unreliability in the roentgenographic diagnosis of tuberculosis. *Am. Rev. Tuberc.*, April, 1954, *69*, 566–584.

The authors have conducted studies to measure the reliability of roentgenographic diagnosis in the

field of tuberculosis; to try to invent a classification of pulmonary lesions as seen on the roentgenograms which would be apt to give optimal reliability; and to measure and prove the validity of such a classification.

It was their opinion that the classification of possibly tuberculous lesions on the basis of roentgenographic appearance is not very reliable. The three approaches to such a classification were as follows: (1) an objective description of the lesion, (2) a quasi-pathologic classification, and (3) a subjective judgment of activity.

This procedure is considered less reliable than the classification of extent in common use (minimal, moderately advanced, far advanced). Actually, the roentgenographic detection of a pulmonary shadow is very much more reliable than attempts at classification.—*J. N. Ané, M.D.*

Sebestény, J., and Erdélyi, M. Über das Mittellappensyndrom. (The middle lobe syndrome.) *Thoraxchirurgie*, June, 1954, *2*, 79–91.

The anatomic and physiological peculiarities of the right middle lobe are discussed, followed by the symptoms and physical findings in "middle lobe syndrome."

Of the 18 cases seen, 3 cases were frankly tuberculous, while in 4 cases tuberculous lymph nodes, in 5 cases nonspecific lymph nodes and in 2 others foreign bodies were found as the etiological factors. In 3 further cases bronchostenosis without external compression was noted. One case could not be clarified. Aimed bronchography and laminagraphy proved very helpful. Bronchogenic carcinoma does not represent an important differential diagnostic possibility, since its incidence in the middle lobe is only 2–3 per cent as compared with the other lobes.

Four cases are discussed in detail.—*Frederick M. Reis, M.D.*

Martin, Joseph E., Jr. Coal miners' pneumoconiosis. *Am. J. Pub. Health*, May, 1954, *44*, 581–591.

Evidence is presented that there is a disease, "coal miners' pneumoconiosis," of the lungs of coal miners which is probably related to their occupation. This statement is based on the extensive studies of Gough in Wales.

This disease is said to have distinctive pathological and roentgenographic characteristics and it can be diagnosed by chest roentgenograms in the presense of an adequate industrial history. The essential feature is the presence of small, more or less circular, discrete, disseminated opacities in the chest roentgenogram. As exposure to coal dust continues, these opacities increase in number and size and to a certain extent in roentgenological density until the whole lung is filled with opacities.

This disease produces progressive disability and is considered to be a preventable disease.—*James J. McCort, M.D.*

Fleischner, Felix G., and Reiner, Leopold. Linear x-ray shadows in acquired pulmonary hemosiderosis and congestion. *New England J. Med.*, May 27, 1954, *250*, 900–905.

Thin horizontal linear shadows occur in the lateral lower lung field of chest roentgenograms of patients with acute or long standing recurrent pulmonary congestion, mainly in patients with mitral valve disease. These lines were first described by Kerley.

In a study of lung sections provided by Dr. Gough of Cardiff, Wales, the authors show these persistent lines to be cast by hemosiderin preferentially appearing alongside and within interlobar septa. In patients with chronic pulmonary congestion these lines may or may not be accompanied by other roentgenologic evidence of pulmonary hemosiderosis. Linear shadows are more frequently observed than the generalized nodularity of the classic picture of far-advanced acquired pulmonary hemosiderosis and apparently reveal a lesser or earlier stage of this condition.

Similar linear shadows are often seen in acute pulmonary congestion. They are fugitive and mostly disappear with recovery from congestive heart failure. Their anatomic substrate apparently is widening of the interlobular septa by edema fluid.—*James J. McCort, M.D.*

Mazzitello, William F. Eosinophilic granuloma of the lung. *New England J. Med.*, May 13, 1954, *250*, 804–809.

Two new cases of eosinophilic granuloma of the lung are reported. The similarity of these pulmonary lesions to the isolated skeletal lesions of eosinophilic granuloma as primary manifestations of the disease is pointed out and a similar chronic benign clinical course is anticipated. In both the author's cases the diagnosis was confirmed by biopsy.

Treatment consisted of ACTH and cortisone. It could not be determined whether these drugs were helpful to the patient.—*James J. McCort, M.D.*

Kunkel, W. Minster, Jr., Clagett, O. Theron, and McDonald, John R. Mediastinal granulomas. *J. Thoracic Surg.*, June, 1954, *27*, 565–574.

The authors report 16 cases of mediastinal granuloma diagnosed by thoracotomy at the Mayo Clinic. Since bacteriological studies could not demonstrate a specific organism, the term "mediastinal granuloma" is used rather than "tuberculoma" which previous authors have been wont to apply. It is emphasized that mediastinal granuloma represents a much more common problem than the paucity of literature would indicate.

While mediastinal granulomas were found in patients from two years to fifty-nine years of age, the lesions were most common in young adults. The majority of the patients were asymptomatic and most often the lesions were found on survey roentgen examination of the chest. Fever, pleuritic pain, and respiratory distress were associated with mediastinal granulomas in a few cases.

The most common roentgenographic feature was the paratracheal involvement. The lesions produced lobular mediastinal widening most prominent on the right side. Some had had a partially calcified periphery and a few had central stippled calcification, which the authors felt, should suggest the diagnosis.

Grossly, most of the tumors were cystic lesions containing necrotic material. They ranged in size from that of a walnut to an orange. A few were solid and contained many small tubercles. In the cystic type, there were fewer tubercles and more fibrosis. Most granulomas appeared to originate in lymph nodes. Material of 13 of the specimens was injected into guinea pigs and none cultured out tubercle bacilli. No specific etiological agent could be proven in any of the cases studied bacteriologically.

The authors studied the symptomatic cases in detail and described the possible dangers of constricting mediastinitis from a ruptured granuloma and associated fibrosis from an unruptured lesion.—*Paul C. Olfelt, M.D.*

Foley, Joseph C., Dreyer, Nicholas B., Soule, A. Bradley, Jr., and Woll, Ephraim. Kerosene poisoning in young children. *Radiology*, June, 1954, *62*, 817–829.

This study is a review of the case reports of 101 children between the ages of eight months and two years of age who had been admitted to hospitals of a community following ingestion of kerosene.

Symptoms included coughing, choking, dyspnea, vomiting, elevated temperature and pulse rate and occasionally drowsiness, stupor or unconsciousness. Death occurred in 1.9 per cent of the cases.

Physical signs in the chest were meager, but rales, rhonchi, and dull areas of percussion were occasionally observed. There was a diagnosis of pneumonitis in 48 cases, all of which showed roentgen changes.

Roentgen findings varied considerably in extent and severity. When pneumonitis appeared, it developed within a few hours after exposure to the toxic agent. The lesions usually consisted of cloud-like densities which were more pronounced in the basal segments. As the process advanced, the individual lesions appeared to enlarge and coalesce. The peak of involvement was reached in two to eight hours. Resolution was gradual and slow.

Transitory signs of cerebral depression were observed in a large number of patients. In order to clarify the conflicting opinion in the literature as to whether cerebral symptoms and pulmonary changes are due to aspiration into the lung or to ingestion into the stomach, the authors have performed experimental studies on rabbits. They have demonstrated that when kerosene is ingested into the stomach no pulmonary changes occur, and only when large amounts are ingested do cerebral symptoms appear. Kerosene injected into the trachea produces marked pulmonary pathology as well as cerebral symptoms.

It is concluded that gastric lavage should not be done after the ingestion of kerosene since it may produce vomiting and pulmonary aspiration. Oxygen therapy and the administration of antibiotics to control secondary infection are of proved benefit.

Emphasis is placed upon the need of educating the public to the dangers to young people from drinking or aspirating kerosene.

Four cases are reported in detail and 13 figures are included.—*E. E. Seedorf, M.D.*

Maassen, Werner. Ein neues Prinzip für die Kontrastmittelapplikation bei der Bronchographie: Der Doppelblockerkatheter. (A new method for application of contrast media in bronchography: a double block catheter.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Feb., 1954, *80*, 229–235.

In the presence of diseases of the lungs, their function often is diminished. As the result, the power of aspiration of the lungs is decreased, so that the demonstration of pathological changes in the upper lobes by bronchography presents difficulties. Before the bronchial system of the upper lobes may be outlined with contrast material completely, there is often a reflux and gravitation of this material into the lower lobes and even into the lung on the other side.

The author describes a method whereby certain bronchial openings are blocked and those desired to be filled are left patent. A catheter has been devised which allows isolated anesthetization of lung bronchi and the aiming of the contrast material either into the upper, middle or lower lobes. The catheter consists of two parallel tubes, one of which ends between the two balloons located in the distal end of the catheter. The other tube terminates just below the lowermost balloon. If the tip of the catheter is inserted into the main bronchus and then gradually pushed more deeply, the bronchi of the middle and lower lobes may be anesthetized extremely well. When the catheter is at the proper height, the opening of the upper lobe may be anesthetized. After these procedures have been accomplished both the balloons are inflated. The upper lobe is filled, after which the material is inserted into the other catheter leading to the middle and lower lobes.

In filling the right side, one may fill the upper lobe alone but on the left side the superior segment of the lower lobe is usually outlined at the same time

as is the upper lobe because of the course of the bronchus to this segment on this side. By the use of the double block method, more pressure is necessary than is usually used, so that better and more complete filling of cavities and fistulae is accomplished. Alveolar or peripheral filling of the lungs does not occur more frequently by this method.—*Samuel Richman, M.D.*

Conde Otero, Francisco, and Torres Cruz, Joaquin. Un nuevo aspecto del lipiodol en broncografías. (A new aspect of bronchography with lipiodol.) *Arch. méd. de Cuba*, May, 1954, *5*, 222–226.

Bronchography with lipiodol has the disadvantage of the oil filling the alveoli and remaining there for a long time, thus hindering the accuracy of further examination, diminishing the respiratory capacity of the lung, and producing inflammatory reaction. Following the technique of Cristini and Tropé, the authors mix 20 cc. of lipiodol with 10 gm. of sulfanilamide obtaining a thick, white, creamy substance that fills bronchi and bronchioli without reaching the alveoli. In 5 cases an excellent outline of the bronchial tree was obtained while the patient had expectorated the contrast medium between twenty-four and forty-eight hours.—*F. Comas, M.D.*

Cotton, Bert H., Penido, J. R. F., Birsner, J. W., and Babcock, Claude E. Coexisting pulmonary coccidioidomycosis and tuberculosis; a review of twenty-four cases. *Am. Rev. Tuberc.*, July, 1954, *70*, 109–120.

Coexisting pulmonary coccidioidomycosis and tuberculosis has assumed new importance with the incidence of coccidioidal infection, especially in endemic areas, in the recognition and treatment. The authors have reviewed the literature and have arranged in table form 19 cases of coexisting pulmonary coccidioidomycosis and tuberculosis along with 24 cases of their own, making an attempt to postulate the pathogenesis and outline the diagnosis and treatment of this combination of diseases.

The result of their findings is that surgery or pulmonary resection is often the treatment of choice in the coexisting coccidioidal and tuberculous disease. In none of the 9 cases reported following surgery did spread of the infection occur postoperatively. In the diagnosis of all pulmonary cavities the possibility of coexisting pulmonary coccidioidomycosis and tuberculosis must be considered. In a patient with a known coccidioidal cavity who develops meningitis, the etiology should be assumed to be tuberculosis. In a known pulmonary coccidioidal infection, if secondary area of infiltration or infection occurs, the most common cause of the new area of disease is usually tuberculosis.—*Thomas E. Padgett, M.D.*

Forsee, James H., and Perkins, Rex B. Focalized pulmonary coccidioidomycosis, a surgical disease. *J.A.M.A.*, July 31, 1954, *155*, 1223–1227.

Fifty cases with localized pulmonary coccidioidomycosis are briefly reviewed and analyzed. All had primary definitive resectional surgery either wedge, segmental or lobectomy. The decisions as to the extent of the resection were reserved pending the findings at the time of exploration as to the size and location of the lesion, whether it was solid or cavitary, and the amount of surrounding parenchymal involvement. Other examinations beside chest roentgenograms were mainly bronchoscopy and skin tests. The bronchoscopic findings included stenosis, ulceration, bleeding and purulent exudate related to the corresponding lobe orifice. Sixty-five per cent showed positive skin tests. Fifteen cases had a definite preoperative diagnosis of coccidioidomycosis, 13 cases were strongly suspected, the rest were undiagnosed, some being mistaken for tuberculosis. There were no operative or postoperative deaths. Only 5 had postoperative complications. One had contralateral spread which cleared completely in seven weeks; 1 had recurrent cavitation which was treated with lobectomy and thoracoplasty with good result; another had recurrent cavitation but refused further surgery; and 2 developed bronchopleural fistulas. On operation and pathological examination the lesions were either solid nodules or cavitary, invariably located peripherally. In cavitary lesions the visceral pleura formed a part of the cavity wall.

Roentgenographically, the typical coccidioidal cavity appeared as a thin-walled, cyst-like, discrete cavity without accompanying visible parenchymal reaction. The solid lesions appeared as round or ovoid densities which could hardly be differentiated from other coin lesions in the lung.

The authors state that surgery is indicated:

1. In solid lesions of unknown cause for diagnostic and therapeutic purposes.

2. In cavitary lesions. Usually collapse therapy, bed rest and drugs are unsuccessful in these cases. Those that are collapsed may reopen. They may involve a lymph node, communicate with and ulcerate into a bronchus or blood vessel so that pathways are open for lymphogenous, bronchogenic and hematogenous spread. The cavity may rupture with resulting pneumothorax, empyema, nonexpansile lung or bronchopleural fistulas.

3. In associated lesions such as bronchiectasis, carcinoma and tuberculosis.—*P. B. Parsons, M.D.*

Kassowitz, Karl E. The pulmonary tuberculoma in childhood; its medical and surgical management. *J. Pediat.*, Aug., 1954, *45*, 153–163.

The author discusses pulmonary tuberculosis in childhood and the role of surgery in the various types of lesions. Four types of parenchymal tuberculomas are described: (1) the primary tuberculoma of minute size; (2) the more or less extensive nodular

residual lesion following post-primary tuberculous meningitis; (3) the reinfection type of isolated tuberculomas; (4) cavitary lesions following reactivation of primary or disintegration of secondary tuberculomas.

There is a basic difference between the residual lesion, after chemotherapy, in the lung parenchyma of the mature person and the peripheral tuberculous process in the lungs at early and mid-childhood. It is the collateral lymphadenitis which represents the main, if not the only, differential feature in childhood and adult tuberculosis. The characteristic feature of primary tuberculosis of the lungs is enlargement of the lymph nodes in the hilus which are never so prominent in other forms of the disease. The prominent role played by the participation of the central tracheobronchial lymph nodes in the primary and post-primary tuberculous process has to be taken into account in considering the therapeutic management of such patients.

Cases are presented which illustrate the four types of childhood lesions mentioned with an evaluation of radical pulmonary resection for each type. The contraindication to the surgical approach of the primary complex rests with the simultaneous involvement of the regional lymph nodes, which does not permit anything like a complete removal of all the important foci except by total pneumonectomy.

The same considerations appear in questioning the validity of resective surgery in the second and third categories which include the post-primary pneumonic lesions with their more extensive nodular residuals and the isolated secondary tuberculomas or coin lesions. In both, the factor of central foci in tracheobronchial lymph nodes which are invariably present would limit any surgical procedure to a subtotal resection.

It is only in the rather exceptional instances of proved cavitary lesions that pulmonary resection should be considered alongside other more conservative and reversible methods of treatment. Bronchogenic dissemination or the improbability of cavity closure under nonresective therapy are strong arguments for surgery. Examples of satisfactory results by both methods are presented. The author favors the more conservative approach even in the rare instances of cavitary lesions in children and feels that the proper identification and classification of isolated nodular lesions in children's lungs will lead to a proper therapeutic program which, as a rule, will be entirely successful without radical surgery. —*James F. Martin, M.D.*

Gay, Brit B., Jr., and Bonmati, José. Primary neurogenic tumors of the lung and interlobar fissures; a review of clinical and radiologic findings in reported cases with addition of two new cases. *Radiology*, July, 1954, *63*, 43–47.

Neurogenic tumors usually arise in the posterior mediastinum. They do, however, occasionally occur primarily in the lung or interlobar fissures. The authors have reviewed 15 cases of neurogenic tumors of the lung and interlobar fissures found in the literature, and have added 2 of their own.

It is stated that neither clinical nor roentgenographic findings are diagnostic. The roentgenograms will usually reveal a well circumscribed, rounded or lobulated, lesion of homogeneous density without calcium content.

Treatment is surgical.—*A. Ralph Watson, M.D.*

Forster, E., Sichel, D., and Roegel, E. Transversoaxial tomography as a valuable help in estimation of operability of pulmonary cancer. *J. Thoracic Surg.*, June, 1954, *27*, 593–602.

The authors note that simple roentgenograms and laminagrams enable us to diagnose and localize pulmonary cancer, but the problem of demonstrating tumor extension to the mediastinum and pulmonary veins is usually not solved by conventional roentgenographic techniques. To clarify the possibility of extension to the mediastinal structures, horizontal laminagraphy was used. Several cases are described and reproductions of horizontal laminagrams show quite well the extension of the tumor to the mediastinal structures.

The authors believe the horizontal laminagrams will give precise information as to the tumor involvement of the vertical intrathoracic organs only, and therefore only in the right chest wall is the method reliable. In the left hemithorax, the heart and aortic arch may appear as one with the tumor because of the oblique positions of the heart and aortic arch. Therefore, the procedure is of less value on the left side.—*Paul C. Olfelt, M.D.*

Jacob, G. Gibt es ein typisches Röntgenbild der klinisch eben manifesten interstitiellen Pneumonie der Frühgeburten? (Is there a typical roentgen appearance of an interstitial pneumonia in premature infants at the beginning of the clinical manifestations?) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, June, 1954, *80*, 697–708.

Seventy-two cases of interstitial pneumonia in newborn premature infants are described with reference to the roentgen aspect of the disease. In 50 per cent of these cases, postmortem examination was available for comparative purpose. Many roentgenological features are considered: Extent and shape of the shadows; type of shadow; compensatory emphysema; pleuritic involvement; position of the diaphragm; pneumothorax; pneumopericardium; heart size; involvement of the hili; plate-like atelectasis. There are 10 reproductions of chest roentgenograms illustrating the different diagnostic points. After considering the various roentgen signs, the following conclusions are reached:

1. Extensive symmetrical hilifugal densities are demonstrable, especially in the upper and middle lung fields; in the first stage there is a more or less homogeneous shadow (edematous stage); in another stage there is more mottling due to atelectasis; yet another stage may show a nodular appearance of densities due to emphysema and atelectasis.

2. There is compensatory emphysema of the lateral aspect of the lower lung fields.

3. The hili are not enlarged.

4. The pleura is not involved.

5. A spontaneous pneumothorax may be present.

6. There may be emphysema of the mediastinum.

7. The diaphragms are low.

8. Often the heart shadow is small.

The author believes that the roentgen appearance of interstitial pneumonia in premature newborns is fairly typical and of considerable help in the clinical diagnosis of this disease.—*Hans W. Hefke M.D.*

Umiker, W. O., and Iverson, Lalla. Postinflammatory "tumors" of the lung; report of four cases simulating xanthoma, fibroma, or plasma cell tumor. *J. Thoracic Surg.*, July, 1954, *28*, 55–63.

The authors describe 4 cases of postinflammatory "tumors" of the lung. Clinically, these cases were characterized by histories of antecedent respiratory infection, and later by roentgenograms suggestive of granulomas or well circumscribed neoplasms. The roentgen findings showed little or no change over long time intervals.

Pathologically, these "tumors" closely simulate true tumors, such as xanthoma, fibroma, xanthofibroma, neurofibroma, vascular tumors and plasma cell tumors. The most important histopathological criteria of postinflammatory tumors are the large number of inflammatory cells, lack of mitotic activity and remnants of pre-existing parenchyma throughout the mass.—*Paul C. Olfelt, M.D.*

Mullard, K. S. Congenital tracheoesophageal fistula without atresia of the esophagus. *J. Thoracic Surg.*, July, 1954, *28*, 39–54.

The author reviews the embryology of congenital tracheo-esophageal fistula with and without esophageal atresia. The published reports of congenital tracheo-esophageal fistula without atresia are summarized and 2 new cases of this condition are reported.

Symptoms of coughing food particles and of recurrent and chronic pneumonitis were frequent. In many cases, the onset of symptoms was late in life. The most accurate method of diagnosis was by roentgen study of the esophagus after swallow of barium or lipiodol. This study should be carried out in the prone position. Bronchoscopy and esophagoscopy frequently failed in demonstrating the fistula that was shown by roentgenologic examination.—*Paul C. Olfelt, M.D.*

Whitfield, A. G. W., Lannigan, R., and Bond, W. H. Fatal post-radiation pneumonitis. *Lancet*, July 17, 1954, *2*, 117–119.

A case of fatal postirradiation pneumonitis is presented. A patient with Hodgkin's disease involving the cervical and mediastinal lymph nodes received a minimum tumor dose of 3,000 r to the mediastinum in 26 days. One month later there was exertional dyspnea which increased in severity during the following month. In spite of oxygen therapy and cortisone the patient died in 72 hours.

At autopsy the lungs showed areas of partial collapse and foci of emphysema. The pleura was thickened in places with underlying fibrosis of the lungs. Microscopically the dominant change was the reduction of total alveolar space associated with fibrosis of the alveolar and capillary walls. A well defined hyaline membrane had formed.—*Lawrence A. Davis, M.D.*

Takahashi, Shinji, and Shinozaki, Tatsuyo. Solidography of the heart. *Acta radiol.*, May, 1954, *41*, 435–440.

A mould of the heart can be obtained by making a series of rotatory cross-section roentgenograms, outlining heart and great vessel contours with flexible lead wire and then pouring plaster into this wire frame, and stacking the resultant plaster layers.

By stacking nineteen films, and exposing half at a time, it is possible to obtain nineteen roentgenograms with only two rotatory exposures.

This is a simpler procedure than the one described about twenty-four years ago by Professor Palmieri, and since it makes possible construction of a very accurate model, it may be of considerable practical value.—*Lois Cowan Collins, M.D.*

Macpherson, I. The clinical approach to mitral disease. *J. Fac. Radiologists*, Jan., 1954, *5*, 155–166.

A patient with rheumatic heart disease some time after the initial attack may have a clinically normal heart, evidence of slight mitral valvular involvement in the form of a systolic murmur alone, pure mitral stenosis, pure mitral regurgitation, or combined stenosis and regurgitation. In most cases of mitral disease, a fairly accurate clinical diagnosis can be made by a correlation of symptoms, physical signs, and electrocardiographic and roentgenological changes. The following classification of mitral disease is suggested:

1. Mitral valvulitis with active rheumatic carditis: This occurs mainly in children and accurate roentgen diagnosis is seldom required in the acute stage.

2. Mitral valvulitis (chronic or healed): This includes cases where, long after all clinical signs of active rheumatic carditis have disappeared, there is still a loud systolic murmur at the apex, with only very slight or no cardiac enlargment. Symptoms are absent or minimal. The electrocardiogram is normal. Roentgenologically the heart is not enlarged and the left auricle is normal in size or only slightly enlarged. The ventricles may be of normal size, but either or both may be slightly enlarged.

3. Pure mitral regurgitation: In this group there is severe mitral regurgitation without any evidence of stenosis. The condition usually presents after a long and benign course with auricular fibrillation and left ventricular failure in later life, *e.g.*, in the fifties. The physical signs are those of left ventricular enlargement with a loud systolic murmur at the apex, a soft first sound, and often a loud third heart sound. Roentgenologically the left ventricle is enlarged and there is a very large left auricle extending to the right, to the left, and posteriorly. The latter shows expansile pulsation in both anteroposterior and oblique views. In the later stages pulmonary congestion is present from left ventricular failure.

4. Mitral stenosis: In the early and mild case the auscultatory signs of mitral stenosis are usually incomplete and consist of a short mid-diastolic mumur, a presystolic murmur or both together. Symptoms are slight or absent. Roentgenologically there are usually no changes except enlargement of the left auricle, and even this may be normal in size. In fully developed mitral stenosis the auscultatory findings show the full picture of a loud first sound, a mitral opening snap and a long diastolic murmur occupying the whole of diastole and running into presystole. Symptoms are mild or absent. Roentgenologically only enlargement of the left auricle with minimal ventricular changes can be seen. In tight mitral stenosis the two criteria for the diagnosis, from a clinical point of view, are: (a) the presence of pulmonary congestion and its associated symptoms and signs; (b) the presence of active pulmonary hypertension, *i.e.*, increased pulmonary arteriolar resistance. In simple uncomplicated tight mitral stenosis seen in relatively younger age groups, characterized by severe exertional dyspnea, recurrent pulmonary edema, and hemoptysis with a small heart, auscultation shows the full signs of mitral stenosis with P-wave changes in the electrocardiogram. Roentgenologically the heart is not enlarged. The left auricle shows some but not gross enlargement. There is evidence of pulmonary congestion at certain periods, but this may be difficult to demonstrate roentgenologically. In mitral stenosis with pulmonary hypertension the symptoms are variable. Some may be free from symptoms while others are breathless on exertion. Right ventricular failure occurs ultimately. Roentgenologically the right ventricle is much enlarged and the right auricle may be enlarged. The main pulmonary artery is enlarged and the hilar branches are prominent. Pulmonary congestion may or may not be present. The left auricle is apt to be large in later stages, particularly with auricular fibrillation.

5. Mitral stenosis and regurgitation: Here the degree of regurgitation is more than slight, making these patients unsuitable for mitral valvulotomy. Weakness and fatigability are common. Auscultation shows a characteristic combination of a long, loud systolic murmur and a short low-pitched diastolic murmur with frequently an opening snap of the mitral valve. Electrocardiographically auricular fibrillation and combined hypertrophy of right and left ventricles are the common findings. Roentgen examination shows considerable cardiac enlargement, with a very large left auricle sometimes showing expansile pulsation. The auricular appendage is usually prominent on the left border. Aneurysmal enlargement of the left auricle to the right is common and expansile pulsation is usually quite evident in the auricle. The left ventricle is enlarged.

6. Complicated mitral disease: The complications are numerous, including active rheumatic carditis, auricular fibrillation, auricular thrombus, heart failure, other valve lesions, and bacterial endocarditis.

In conclusion, the author states that by studying a combination of symptoms, physical signs and electrocardiographic and roentgenological changes it is possible to make a fairly accurate diagnosis in patients with mitral disease. Roentgen examination is often quite helpful with regard to hypertrophy of the ventricles, enlargement of the left auricle, and the state of the pulmonary vessels.—*Samuel G. Henderson, M.D.*

Steiner, Robert E., and Goodwin, John F. Some observations on mitral valve disease. *J. Fac. Radiologists*, Jan., 1954, *5*, 167–177.

In this article the authors deal briefly with the varying appearance of the left auricle, with the roentgenological diagnosis of mitral incompetence and with the pulmonary vascular pattern in mitral valve disease, in conjunction with the clinical findings. The findings are based on a clinical and roentgen study of 91 patients, a number of whom have been submitted to mitral valvotomy. Special investigations in selected cases consisted of cardiac catheterization, laminagraphy of the heart, angiocardiography, microscopic examination of the pulmonary vessels in specimens of lungs obtained at operation by lingular biopsy and postmortem arteriograms. The clinical criteria for the diagnosis of mitral incompetence were considered to be: enlargement of the left ventricle in the absence of any other cause for this, a loud early or mid-systolic murmur at the apex conducted into the axilla, a soft apical first heart sound, and an absent or faint opening snap of the mitral valve.

The left auricle was found to vary greatly in size. In the authors' view the degree of valvular stenosis is not directly proportional to the size of the auricle. The very large or aneurysmal auricles are nearly always associated with a significant degree of mitral regurgitation. Only rarely is a very large auricle associated with pure mitral stenosis. Angiocardiography gives additional information about the appearance and size of the left auricle and confirms the impressions gained from a straight posteroanterior roentgenogram. In the writers' angiocardiographic studies no significant differences were found between the filling time and density of the left auricle and ventricle in patients with predominant or pure mitral stenosis, on the one hand, and in patients with mitral stenosis associated with predominant mitral incompetence, on the other.

An exact roentgenographic diagnosis of the degree of mitral incompetence is not always possible in the presence of mitral stenosis, and the authors consider that, at present, the most reliable roentgenological sign is the size of the left auricle, which in most instances is grossly enlarged. An auricle which forms the greater part of the right cardiac contour on the straight posteroanterior films and also shows a very prominent left auricular appendix in addition to considerable esophageal displacement is almost always associated with clinical signs of mitral incompetence. Associated left ventricular enlargement is only suggestive of mitral incompetence in the absence of any other cause, such as significant aortic valve disease or hypertension.

Expansile pulsation of the left auricle in all directions on fluoroscopy, although occurring in mitral incompetence, particularly in its pure form, is also frequently seen in mitral stenosis with minimal incompetence. It is merely a sign of mitral valve disease and not a guide to the degree of regurgitation.

Two patients in the group studied had extensive left auricular calcification. This complication of rheumatic heart disease is rare. The incidence of valvular calcification in rheumatic heart disease is high. Of 48 patients who died from mitral valve disease, over a four year period, none had any evidence of auricular calcification, but in 25 the mitral valve, and in 13 the aortic valve were calcified. Of the 91 patients studied in this series, 2 had demonstrable evidence of auricular calcification, 19 had mitral valve calcification and 4 had aortic calcification. In the authors' series none of the cases with heavy valvular calcification had any clinical or roentgenological evidence of significant mitral incompetence, nor was this found at operation or autopsy. Calcified valves have been operated on successfully and their roentgenological demonstration need not be a contraindication to operation. A preoperative roentgen diagnosis of valvular calcification is important because it tells the surgeon what to expect at operation.

In many patients the pulmonary vascular pattern, with the exception of varying degrees of enlargement of the main pulmonary arteries, is normal. In some the pulmonary arterial pressure is normal, while in others the pulmonary arterial pressure is elevated and in these the pulmonary vascular pattern is abnormal. Two types of pulmonary hypertension have been recognized: (1) passive pulmonary hypertension, which is the result of increased left auricular and pulmonary venous pressures, associated with only a slight elevation in the pulmonary arterial pressure; (2) active pulmonary hypertension, which is the result of an increase in the pulmonary arteriolar resistance and is associated with higher pressures.

To further study pulmonary hypertension the authors have investigated the pulmonary vascular pattern by venous angiocardiography and by selective pulmonary arteriography. In patients with active pulmonary hypertension there is considerable enlargement of the pulmonary arterial trunk and of the main branches, associated with a significant degree of right ventricular hypertrophy. There is a striking diminution of the smaller arterial branches, particularly at the bases of the lungs and in the peripheral lung field. Only the main arteries and veins are enlarged, the smaller arteries and arterioles being narrowed, and some of the peripheral pulmonary shadows seen on the posteroanterior roentgenograms are nonvascular and due to other causes.

The pulmonary vascular pattern of pulmonary hypertension is in marked contrast to that seen in patients with pulmonary venous congestion, but without active hypertension. In these circumstances there is no sudden change in the caliber of the distended and dilated pulmonary arteries, which appear engorged right out into the peripheral lung field, concomitant with venous engorgement and the frequent presence of pleural transudates. There is some direct correlation between the degree and extent of narrowing in the smaller pulmonary arteries with the level of the pulmonary arterial pressure as measured by cardiac catheterization. The changes in the small pulmonary arteries revealed by angiocardiography can also be detected by careful examination of plain roentgenograms. It is difficult to assess accurately the size of the main pulmonary artery on the plain posteroanterior teleroentgenogram in the presence of moderate or considerable cardiac enlargement, but angiocardiography permits a more accurate estimation. In the authors' experience, the size of the main pulmonary artery correlates well with the degree of pulmonary hypertension when this is moderate or severe. There is no correlation between left auricular size and the degree of pulmonary hypertension. There are probably two factors responsible for active pulmonary hypertension. There is evidence of vasoconstriction of the smaller arteries and arterioles, and there is also organic arterial narrowing due to endothelial hypertrophy and atheroma.

Pulmonary hemosiderosis is not an uncommon complication of mitral stenosis, being diagnosed in

25 per cent of the patients in this series. The degree of involvement was variable and consisted mainly of rather coarse, well-circumscribed stippling in the peripheral lung fields, usually but not always associated with pulmonary hypertension. The authors did not see any case which presented diffuse miliary mottling. In a large number of patients, in the lower zones of the lungs toward the periphery, the authors have noted some fine, horizontal linear shadows which were most marked in patients with pulmonary hypertension and congestive cardiac failure. The significance of these shadows has not yet been determined. They tend to be transient and often disappear after a successful mitral valvotomy. Kerley ascribes them to subpleural lymphatics or to interstitial edema. The authors' postoperative follow-up studies are not yet sufficiently extensive to permit assessment of changes in the heart and lungs after valvotomy, but so far they have not noted any significant change in heart size.—*Samuel G. Henderson, M.D.*

Whitaker, William, and Lodge, Thomas. The radiological manifestations of pulmonary hypertension in patients with mitral stenosis. *J. Fac. Radiologists*, Jan., 1954, *5*, 182–188.

Pulmonary artery blood pressures in patients with mitral stenosis range from normal to levels higher than the pressures in the systemic arteries. In such patients several observers have attempted to relate pulmonary hypertension to roentgenological abnormalities in the heart and lungs. Numerous investigators have noted enlargement of the right ventricle and of the main pulmonary artery and its proximal branches roughly corresponding to the degree of pulmonary arterial hypertension. The purpose of the present study is to make an objective assessment of the relation between roentgenological abnormalities and pulmonary hypertension in patients with mitral stenosis.

Twenty-five patients with mitral stenosis as their sole or dominant lesion were studied. One of the authors recorded the pulmonary artery blood pressures by means of cardiac catheterization, and the other reported the roentgenological abnormalities without knowledge of the pressure records. The pulmonary artery blood pressures were recorded with the tip of the catheter in the main pulmonary artery and the pulmonary capillary blood pressures with the tip of the catheter wedged in a small branch of a pulmonary artery. The roentgenological features were reported from a posteroanterior chest roentgenogram taken within a few days of the cardiac catheterization. The roentgenograms were not all taken on the same apparatus, but the standard technique was 20 milliampere seconds, 55 kv. (peak) at 60 in. distance for a patient of average size, varying the kilovoltage from 50 to 65 according to the build. On reading the films, an assessment was made of the following seven features: (1) heart size, graded as normal up to 4 plus; (2) the "pu'monary conus," represented by a convex portion of the middle arc of the left border of the heart immediately above the ventricular shadow as seen on a posteroanterior film; (3) the main pulmonary artery as seen on the left border of the cardiovascular shadow just below the arch of the aorta and above the conus; (4) the right and left main branches of the pulmonary artery as seen in the respective hili (Assmann regards a width of the main pulmonary artery in the hilus of less than 10 mm. or more than 14 mm. as being pathological); (5) the perihilar vessels, which are the main lobar trunks emerging from the main branches of the pulmonary artery in the hili seen immediately outside the hilar regions in the middle third of both lungs; (6) the peripheral vessels, seen in the peripheral thirds of both lungs, mostly arteries rather than veins and branches of the pulmonary artery rather than of the bronchial systemic circulation; (7) horizontal lines, chiefly seen in the outer parts of both lower lobes, occurring as short, nonbranching, roughly horizontal lines passing inwards from the pleural margin of the lung for a distance of up to ½ in. The cause of these shadows has not been proved. Possibly they are due to congested subpleural lymphatics.

In this series pulmonary hypertension was arbitrarily considered mild in 7 patients with pulmonary artery mean blood pressures less than 40 mm. Hg, moderate in 10 patients with pressures from 40 to 69 mm. Hg, and severe in 8 patients with pressures of 70 mm. Hg or over.

No relation was found between the degree of cardiac enlargement and the degree of pulmonary hypertension, since in all three groups with mild, moderate or severe pulmonary hypertension, there were patients with slight, moderate or marked cardiac enlargement. It is suggested that a heart of normal size in a patient suffering from mitral stenosis excludes moderate and severe pulmonary hypertension, because only in the group of patients with mild pulmonary hypertension was the heart size normal. There was enlargement of the "pulmonary conus" of the right ventricle in 3 of 8 patients with severe pulmonary hypertension, in 8 of 10 patients with moderate pulmonary hypertension and in 6 of 7 patients with mild pulmonary hypertension, showing that the presence or absence of "conus" enlargement is no guide to the degree of pulmonary hypertension. The main pulmonary artery was enlarged with all degrees of pulmonary hypertension, making enlargement of the pulmonary artery a sign of little value in determining the degree of pulmonary hypertension. It is concluded that a roentgenologically normal main pulmonary artery excludes severe pulmonary hypertension and suggests normal pressure in the pulmonary artery of such patients. Gross enlargement of the main branches of the pulmonary

artery excludes mild pulmonary hypertension and suggests severe pulmonary hypertension in a patient suffering from mitral stenosis. Normal main branches of the pulmonary artery were seen in 3 of 7 patients with mild pulmonary hypertension, in 3 of 10 patients with moderate, and in no patient with severe pulmonary hypertension, suggesting that such a normal appearance contraindicates severe pulmonary hypertension. However, this does not exclude moderate or mild pulmonary hypertension or assist in differentiating between these two latter degrees of pulmonary hypertension. The frequency of enlargement of the main branches of the pulmonary artery with all degrees of pulmonary hypertension was such as to make enlargement of these branches of no diagnostic importance in assessing whether pulmonary hypertension is mild, moderate or severe in a patient with mitral stenosis. The perihilar vessels were enlarged in caliber and increased in number in some of the patients in the 3 groups with mild, moderate or severe pulmonary hypertension. These changes are regarded as of little use in the assessment of the degree of pulmonary hypertension in a patient with mitral stenosis. An increase in number of peripheral pulmonary vessels is a sign of moderate or severe pulmonary hypertension. The increase in number of peripheral pulmonary vessels may be casually related to an increase in pulmonary capillary blood pressure, but it may equally well be related to an increase in pulmonary artery blood pressure. Horizontal lines, noted above, are believed to represent a sign of moderate or severe pulmonary hypertension. In the present series all the patients who had an increase in number of peripheral pulmonary vessels also had horizontal lines, suggesting that these two signs are manifestations of the same functional disturbance which may well be an increase in pulmonary venous blood pressure, although it can equally well be the increase in pulmonary artery blood pressure.

The authors conclude that it is apparent from the roentgenological abnormalities in the heart and lungs of a patient suffering from mitral stenosis that it is possible to recognize complicating pulmonary hypertension, and in many patients it is also possible to assess the degree of pulmonary hypertension.—*Samuel G. Henderson, M.D.*

Hallerbach, H. Zur angiokardiographischen Darstellung der Pulmonalstenose. (Angiocardiographic demonstration of pulmonic stenosis.) *Röntgen-Blätter*, June, 1954, *7*, 209–224.

Pulmonic stenosis (valvular stenosis, hypoplasia of the pulmonary artery, and infundibular stenosis) can occur as an isolated defect or in conjunction with other congenital cardiac anomalies of which ventricular septal defect, atrial septal defect, and tetralogy of Fallot are the commonest. The presence of pulmonic stenosis can be, in general, easily established by clinical findings, routine roentgen study, and by heart catheterization. The exact type and extent of the stenosis should be determined, however, in all cases prior to surgery, particularly when direct pulmonary valvulotomy is proposed. Angiocardiography provided such information in over 300 cases of pulmonic stenosis studied by Hallerbach at Professor Janker's Röntgeninstitut in Bonn.

Angiocardiography, attained by peripheral venous injection of contrast medium, served quite well in most cases. For demonstration of the pulmonic stenosis the author used mainly the direct anteroposterior projection instead of the left anterior oblique preferred in the United States. He justifies the use of the sagittal projection by three observations: (1) In cases of pulmonic stenosis where the aorta is transposed (*e.g.* tetralogy of Fallot) the aorta and pulmonary artery lie side by side in the anteroposterior projection and not behind one another as in the normal heart or cases without aortic transposition. (2) In pulmonic stenosis there is more or less enlargement of the right ventricle with displacement of its outflow tract to the left. Therefore the entire "pulmonic stem" is projected free along the left heart border in the anteroposterior view. (3) Rotation of the heart to the left because of right ventricular enlargement secondary to pulmonic stenosis projects the "pulmonic stem" to the left as seen in the anteroposterior view. This rotation can be produced or increased artificially by turning the patient in a very slight right anterior oblique position.

Essential for the exact delineation of the course and dimensions of the pulmonic complex (outflow tract of right ventricle, pulmonic valve area. pulmonary artery) is opacification of these structures in many phases of cardiac activity. For this purpose serial roentgenography or roentgen cinematography is necessary. Three exposures per second suffice, but roentgen cinematography will allow as many as 24 exposures per second, which is preferable. The importance of a large number of serial exposures in a short period of time is graphically illustrated by several cases which demonstrate the great difficulty in differentiating infundibular stenosis from a normal left pulmonary artery descending branch in the anteroposterior projection. The infundibulum fills from below while the left pulmonary artery descending branches fill from above—this differential point can best be established by short-interval angiocardiograms.

A further refinement of technique consists of the use of a filming apparatus by which simultaneous exposures at right angles to each other can be produced, *i.e.*, anteroposterior and lateral serial roentgenograms with one injection of contrast medium.

Despite all of these aids (correct positioning of the patient, multiple serial roentgenograms, and biplane simultaneous exposures), venous angiocardiography does not always yield a clear delineation of cardiac structures. In cases of pulmonic stenosis where there exists a right to left shunt, the left heart is contrast

filled at the same instant as the right heart and overlapping of pulmonic complex structures by the left atrium or aorta may occur. To obviate this complication selective pulmonic angiography can be performed. By this method a large caliber heart catheter is placed under fluoroscopic guidance just beneath the area of stenosis in the pulmonic region and contrast medium injected under pressure through the catheter. Serial roentgenograms are exposed during the injection. The technique leads to a dense concentration of contrast medium in the right ventricle and pulmonic complex only, there being no danger of opacification of other cardiac structures which might hinder demonstration of the area of pulmonic stenosis. Septal defects and aortic transposition associated with the pulmonic stenosis may not be demonstrated by selective pulmonic angiography, therefore accurate diagnosis of the type of congenital cardiac disease present should be made prior to the selective pulmonic angiographic study.

The author illustrates his exposition with multiple excellent examples of angiocardiographic and selective pulmonic angiographic demonstrations of pulmonic stenosis.—*Harold Fulton, M.D.*

Gøtzsche, Henning, and Falholt, Walther. Ebstein's anomaly of the tricuspid valve; a review of the literature and report of 6 new cases. *Am. Heart J.*, April, 1954, *47*, 587–603.

Ebstein's anomaly of the heart has excited some interest recently because of the similarity of its clinical findings to those of more common congenital cardiac defects, particularly pulmonic stenosis with associated atrial septal defect. The authors review the literature and find 16 cases previously reported in which there had been adequate electrocardiographic and roentgenologic studies. They add 6 cases of their own, making a total of 22 cases for critical analysis.

In Ebstein's anomaly there is a malformation of the right atrioventricular ostium. In most cases deformed leaflets of the tricuspid valve are displaced toward the apex of the heart. Physiologically, therefore, the right ventricle is divided into a thin-walled portion incorporated into the right atrium, and a small functioning right ventricle with decreased ability to transport blood from the right atrium to the pulmonary artery.

The *in vivo* diagnosis had been made in only 5 of the 16 cases extracted from the literature, but was apparently possible in all of the authors' examples. Cardiac complaints were elicited in all cases, dyspnea being a constant symptom. Acyanotic cases are extremely rare; in all cyanotic cases the presence of an associated atrial septal defect with veno-arterial shunt was proved by cardiac catheterization, angiocardiography, or postmortem examination. Clinical signs of Ebstein's anomaly are not characteristic of the disease, most cases exhibiting a systolic and diastolic murmur in the lower precordium, but no other conclusive physical feature; the roentgenologic aspects are therefore quite important and can be summarized: (1) the heart is usually enlarged, (2) the left cardiac border is convex and elevated ("square-shaped heart"), (3) the hilar vascular markings may be normal or faint, (4) the pulmonary arch is usually of average prominence, and (5) fluoroscopic observation or roentgen kymography may demonstrated ventricular pulsations only in the "conus" portion of the right ventricle, atrial waves being present in the lower part of the left heart border in the anteroposterior view.

Electrocardiography has the pattern of right bundle branch block (21 of 22 cases). Enlarged P-waves and prolonged atrioventricular conduction are also common.

Seven of the reviewed cases and the authors' 6 cases were submitted to cardiac catheterization. The optimum information to be gained from such study is: (1) demonstration of a large right atrial cavity by conformity of the catheter to the inner wall of the atrial chamber, (2) direct catheterization of an atrial septal defect or evidence of its presence by the demonstration of an arteriovenous shunt between the atria, (3) catheterization of the right ventricle and pulmonary artery may be unusually difficult to accomplish due to the abnormal nature of the tricuspid valve and small size of the functioning right ventricle. If possible, however, this should be done, as the demonstration of a normal right ventricular pressure is expected in Ebstein's anomaly and rules out pulmonic stenosis, a point important in differential diagnosis.

Angiocardiography was preformed in 7 of the earlier cases and in 2 of the authors' cases. Considerable enlargement of the right atrium is shown, delayed emptying of the right atrium and right ventricle may be noted, and delayed, insufficient, or lack of opacification of the pulmonary artery may occur. The atrial septal defect may be demonstrated.

It is concluded that the diagnosis of Ebstein's anomaly is possible during life. The clinico-roentgenologic picture can suggests the diagnosis, but angiocardiography and cardiac catheterization are diagnostically essential.

The diagnosis of Ebstein's anomaly is based on the following criteria:

(1) Signs of pulmonic stenosis on roentgenographic examination (faint hilar vascular markings) or angiocardiography (delayed emptying of the right side of the heart and poor filling of the pulmonary arteries).

(2) Exclusion of pulmonic stenosis by cardiac catheterization.

(3) Evidence of enlargement of the right atrium with distal displacement of the atrioventricular (tricuspid) valve during cardiac catheterization or by angiocardiography.

Confirmatory diagnostic features are, if present:

(4) The presence of the atrial septal defect with

veno-arterial shunt in the absence of pulmonic stenosis.

(5) Ventricular pulsations in the "conus" portion of the right ventricle only, indicating a diminished function of the right ventricle.

(6) Right bundle branch block in cases with or without atrial septal defect.

According to these criteria Gøtzsche and Falholt have found 6 cases of Ebstein's anomaly among approximately 700 catheterized cases of congenital heart disease.—*Harold Fulton, M.D.*

Pedersen, Asger, and Therkelsen, F. Cor triatriatum: a rare malformation of the heart, probably amenable to surgery. *Am. Heart J.*, May, 954, *47*, 676–691.

The term cor triatriatum has been applied to a congenital malformation of the heart in which a transverse band or septum stretches across the left atrium, separating the opening of the pulmonary veins from the mitral orifice. The authors review the literature and add a further case in which mitral valvular disease was suggested from clinical and physiological studies (cardiac catheterization). Thoracotomy revealed a normal mitral valve, and the true condition (cor triatriatum) was recognized only at postmortem examination.

Twenty-two cases of cor triatriatum of the type exhibiting a membranous septum which is either imperforate or perforated by a single or multiple ostia are analyzed. Most patients die in early childhood; those who survive show no characteristic clinical picture. Symptoms are those of pulmonary hypertension and congestion with subsequent right heart failure. Neither stethoscopy, electrocardiography, nor roentgenology yield diagnostic signs. In 8 cases in whom the roentgenologic aspects are reported the heart was diffusely enlarged, in some cases almost globular in shape. Pulmonary hilar congestion was present. Left atrial enlargement was not a constant feature. Angiocardiography, according to the authors, has not been applied to the problem. Cardiac catheterization in their case yielded results strongly suggestive of mitral valvular disease although an apical diastolic murmur and left atrial enlargement were not present.

It is emphasized that this disorder, however rare, should be taken into consideration in obscure cases of pulmonary hypertension, especially when a high "pulmonary capillary" pressure has been measured. Direct pressure measurements at thoracotomy could show hypertension in the pulmonary veins and a normal left atrial pressure, making the diagnosis possible before the heart is opened. This is of importance as the usual cardiotomy incision for mitral valvulotomy will probably not permit detection of the anomalous transverse left atrial septum; exploration by the pulmonary vein approach could demonstrate the defect, however, and theoretically either the septal openings could be enlarged or the septum resected. Apparently no case of this rare anomaly has as yet been surgically attacked.—*Harold Fulton, M.D.*

McKim, J. S., and Wiglesworth, F. W. Absence of the left pulmonary artery; a report of six cases with autopsy findings in three. *Am. Heart J.*, June, 1954, *47*, 845–859.

Six cases of absence of the left pulmonary artery, 3 proved at autopsy, have been studied by the authors. The literature is reviewed and 11 previously reported cases of absence of the right or left pulmonary artery commented upon.

The anatomical features of the anomaly can be explained embryologically on the basis of Congdon's work (Congdon, E. D. Transformation of the aortic-arch system during the development of the human embryo. *Contrib. Embryol.*, 1922, *14*, 47–110). The central or heart-end of the left pulmonary artery fails to develop while the intrapulmonary portion of the pulmonary artery persists. Blood supply to the left lung is by an anomalous obliterated vessel running from the aortic arch system to the hilus of the lung where it becomes continuous with patent, normally distributed, elastic intrapulmonary arteries. In cases of absence of the left pulmonary artery the anomalous obliterated vessel is thought to represent the ductus arteriosus arising from the *left* innominate (a right aortic arch is usually present in association with an absent left pulmonary artery).

The diagnosis of an absent right or left pulmonary artery may be first suggested by plain roentgenograms of the chest which show the hemithorax on the affected side to be somewhat smaller than that of the normal side. The affected lung may appear undervascularized as compared to the opposite lung. This latter picture can be simulated, however, by other anomalies, particularly pulmonic stenosis, when one lung may be undervascularized as compared to the other because of an unequal distribution of collateral circulation, the pulmonary arteries being both present.

The clinical signs of the anomaly are not characteristic, the defect being compatible with life and the patient may be entirely asymptomatic. Many patients have associated serious congenital cardiac defects (patent ductus arteriosus, tetralogy of Fallot, Eisenmenger's complex, etc.) which present their own clinical features.

Angiocardiography gives valuable information, demonstrating a normal appearance of one pulmonary artery and complete absence of the other. The method may fail, however, as in one of the authors' cases where presumably an adequate collateral circulation allowed contrast filling of the intrapulmonary branches of the pulmonary arteries, though the central portion of the left pulmonary artery was absent.

The physiologic significance of absence of a pulmonary artery is that the lung, deprived of its pulmonary circulation, does not participate in oxygen exchange, In the case studied by Madoff and associ-

tes (Madoff, I. M., Gaensler, E. A., and Strieder, J. W. Congenital absence of the right pulmonary artery. *New England J. Med.*, 1952, *247*, 149–157), the affected lung was responsible for only 6 per cent of the oxygen uptake, although it handled 37 per cent of the inspired air. Thus when the single pulmonary artery is clamped or cut off, the patient is immediately deprived of oxygen, unless an adequate bronchopulmonary anastomosis has developed.

It is concluded that "from a surgical standpoint, it would be prudent, when contemplating an aorticopulmonary anastomosis or a pulmonary resection, to be reasonably certain that there is a pulmonary artery both on the operative as well as on the nonoperative side."—*Harold Fulton, M.D.*

Abdomen

Corsellas, M. F., and Durán, Jorge A. Estudio radiológico differencial entre la úlcera y el cáncer gástrico. (Differential roentgen diagnosis between gastric ulcer and cancer.) *Prensa méd. argent.*, July 16, 1954, *41*, 2063–2081.

In most cases the roentgen examination of a gastric ulceration does not allow a clear-cut differentiation between benign gastric ulcer and cancer. Extraluminal and multiple niches are usually benign, while intraluminal filling defects are in most cases malignant. An ulceration in the antrum has to be considered with a high degree of suspicion, and a gastric ulceration that does not heal after four or six weeks of medical treatment should be treated surgically since the chances that it is malignant are overwhelming.—*F. Comas, M.D.*

Dolin, Simon, Mathews, Hugh H., and Russo, Peter E. Congenital obstruction of the duodenum and malrotation of the colon. *Radiology*, July, 1954, *63*, 85–90.

Two cases of congenital extrinsic obstruction of the third part of the duodenum are presented. In both cases there was a faulty mesenteric attachment and malrotation of the colon, resulting in a volvulus of the midgut and an extrinsic obstruction of the distal duodenum.

The embryology is discussed and the development of the obstruction is described.

The necessity for early diagnosis is emphasized. This is accomplished by means of plain roentgenograms revealing a gas filled and dilated duodenum and malpositioned colon. Contrast medium then demonstrates the site of obstruction.—*E. E. Seedorf, M.D.*

Ivie, Joseph McK., and Beveridge, John H. Roentgenologic problems in ulcers about the pylorus. *South. M. J.*, June, 1954, *47*, 530–537.

The authors discuss the interesting problem of ulceration about the pylorus. They believe that the importance of the exact location of the ulcer cannot be overemphasized. The immediate surgical treatment depends largely on the location of the ulcer niche. There is a certain small percentage of the cases in which the ulcer is so close to the pylorus that at the initial roentgenologic examination it is impossible to be certain whether the ulcer is gastric or duodenal. The differential diagnosis between ulcerated carcinoma, benign prepyloric ulcer, hypertrophy of the pyloric muscle and a duodenal ulcer is made difficult because the site of the pyloric ring cannot be determined.

The discussion in this paper is concerned primarily with the location of acute ulceration in the pyloric area. The authors elucidate this with 6 cases in which follow-up examinations after a short interval of intensive medical treatment demonstrated that all of the acute ulcerations thought to be in the pylorus or on the gastric side of the pylorus actually were in the duodenum. They feel that spasm accounts chiefly for the deformity of the pyloric canal and the duodenal cap.

The fact that a gastric ulceration is situated in the prepyloric region of the stomach does not necessarily mean that it is likely to be malignant as in any other part of the stomach but, on the other hand, ulceration in the duodenal bulb is almost always benign. Coupling this with the strong feeling of many surgeons that all gastric ulcers should be treated by surgical resection, the task of exact localization of these peripyloric ulcerations is of such importance that re-examination after medical treatment should be insisted upon in all instances.—*Thomas D. Allison, M.D.*

Swartzbach, Saul, and Curtin, Jerome E. Rupture of the stomach, spleen, and left hemidiaphragm. *A.M.A. Am. J. Dis. Child.*, May, 1954, *87*, 616–620.

The authors know of no previous case report of ruptured stomach, spleen and diaphragm. Their patient was a boy, five years of age, who was admitted to the hospital having been run over by an automobile. He was first seen in the accident room complaining of severe abdominal pain. He had not vomited and was alert and cooperative. However, he was pale, cold, sweaty, and in early shock. An upright roentgenogram of the abdomen showed air beneath each side of the diaphragm, elevation of the left hemidiaphragm, absence of a splenic shadow and a slight pneumothorax on the left side.

At operation, on opening the abdomen much free fluid was found containing blood and stomach contents, together with a large amount of whole and partially chewed peanuts. The spleen was found to be ruptured and bleeding profusely and, therefore, splenectomy was performed. The stomach was then examined and a hole about 10 cm. in diameter was seen in the region of the fundus. The rent was closed. It was noted that the left hemidiaphragm was lacerated and this was closed. The patient recovered

after having had a complicating left empyema. He was readmitted about six weeks later with intestinal obstruction and at operation numerous adhesions, some dense and some filmy, involving the small intestine and peritoneum were found. The patient when last seen was ambulatory and was eating well, and was attending regular classes at school.

The authors state that this case illustrates a combination of surgical problems which is rare. Any one in a child of five years is of serious import. Of interest, also, is the foreign body reaction in the abdomen secondary to the peanuts. This reaction was seen in the microscopic slides of the appendix. The value of upright roentgenograms of the abdomen is emphasized.—*Ralph S. Bromer, M.D.*

Cancelmo, J. James, Jr. Interstitial gastric emphysema, with report of a case. *Radiology*, July, 1954, *63*, 81–84.

Gastric emphysema is a rare condition characterized by air within the walls of the stomach and a few vague symptoms or none at all. Few cases have been reported.

The author reports a case of gastric emphysema which developed in a patient with carcinoma of the esophagus, following a bout of vomiting and attempted intubation of the stomach. Roentgenograms revealed a linear, radiolucent shadow outlining the stomach and separate from the gastric air bubble.

The interstitial emphysema in this patient is attributed to an incomplete or partially walled-off perforation of the esophagus. The postoperative vomiting, which increased the intraluminal pressure, probably forced air through this perforation into the esophageal wall. Subsequently this air dissected its way down into the wall of the stomach.

This condition is to be distinguished from cystic pneumatosis and from emphysematous gastritis.—*A. W. Sommer, M.D.*

Olson, John D. Pneumatosis cystoides intestinalis; report of a case. *A.M.A. Arch. Surg.*, June, 1954, *68*, 899–906.

Pneumatosis cystoides intestinalis, also known as gas cysts of the intestine, is a rare pathological condition. Fewer than 50 cases are recorded in the American literature.

The condition is a collection of multiple thin-walled, gas-filled cysts, varying in size from a few millimeters up to several centimeters in diameter. They are usually located in a specific segment of the intestinal tract, occurring most commonly in the small intestine and quite frequently in the terminal ileum. In adults, they are usually located subserosally, but may extend into areolar tissues of the mesentery and extraperitoneal areas. In infants, the cysts are usually submucosal. The etiology is indeterminate but may be of mechanical or dietary nature.

The gas cysts may be demonstrated by roentgenologic examination. The authors report such a case.

The treatment is surgical removal, especially if in a localized portion of the intestine or if the cysts are producing obstruction due to encroachment into the lumen of the intestine.—*C. Peter Troug, M.D.*

Wellman, G. O., and Haines, Richard D. Lymphosarcoma of the gastrointestinal tract. *South. M. J.*, June, 1954, *47*, 573–577.

The authors present a study of 25 cases of lymphosarcoma of the gastrointestinal tract. These represent approximately 2 per cent of the series of 1,210 primary malignant neoplasms of the upper gastrointestinal tract. The cases of systemic lymphosarcoma have been excluded.

In this group 60 per cent were males. The average age was forty-six with a range from six to eighty-two years. The general clinical picture revealed the average duration of symptoms was 10.1 months. On admission 48 per cent of the patients had a palpable abdominal mass. At exploration 20 of the patients of this group had metastases beyond the site of the primary lesion, and 6 patients had multiple primary lesions.

Lymphosarcoma of the stomach accounted for 52 per cent of the cases in this series. In this group 8 of the 13 patients had ulcer-like symptoms. A palpable mass was present in 6 patients. Only 1 patient had hematemesis. The roentgenographic findings are not indicative of the cell type of malignancy in the stomach but the authors point out that multiple polypoid filling defects or presence of giant rugae with a localized gastric ulcer favor lymphosarcoma over carcinoma.

In this series and in a general review of the literature it was evident that five year survival for lymphosarcoma of the gastrointestinal tract was uncommon, regardless of the therapy employed. Surgery and irradiation together gave fair palliation. The only five year survival, without clinical evidence of recurrence, was treated with irradiation alone.—*Thomas D. Allison, M.D.*

Connell, Thomas H., Jr., and Bogin, Maxwell. Gangrene of the intestine occurring in utero; report of successful resection. *A.M.A. Am. J. Dis. Child.*, May, 1954, *87*, 621–625.

A case is presented in this paper of gangrene of the small intestine occurring in utero which resulted in perforation and meconium peritonitis. Severe ascites was present at birth which necessitated immediate operation. The mechanical factor precipitating the perforation was gangrene of the upper ileum, apparently due to a segmental volvulus. The operation was performed when the infant was two hours old.

Roentgen examination of the abdomen, one hour after birth, before operation, showed homogeneous opacity in the abdomen, characteristic of marked ascites, with a small amount of gas in the stomach

and upper intestine. This gas was less than that customarily found one hour after birth. No pneumoperitoneum was noted. The intestine was resected and an end-to-end anastomosis carried out, The patient received vigorous postoperative therapy, including whole blood transfusions, cortisone, antibiotics, and parenteral fluids.

At the age of thirteen months when the child was examined, she seemed to be entirely normal, physically and mentally and manifested no peritoneal calcification.—*Ralph S. Bromer, M.D.*

Fleischner, Felix G., Mandelstam, Paul, and Banks, Benjamin M. Roentgen observations of the ileostomy in patients with idiopathic ulcerative colitis. I. The well functioning ileostomy. *Radiology*, July, 1954, *63*, 74–80.

In order to better evaluate the problems in the study of immediate and late postoperative ileal dysfunction, a study of the well functioning ileostomy was undertaken. Thirteen patients with ileostomies done for the treatment of severe idiopathic ulcerative colitis were studied. Eleven had had partial or total colectomy also. Periods varying from six months to seven years had elapsed since their last episode of ileostomy dysfunction.

The prestomal ileum was studied both by barium enema through the ileostomy stoma and by oral ingestion of barium. Patients with well functioning ileostomies demonstrated a normal transit time for orally administered barium. The motility pattern of the small intestine was normal. The lower ileum was found capable of inspissating its contents with the formation of fecal matter even though the colon had been removed.

The prestomal ileum, visualized by barium enema through the ileostomy, was normal in width and contour and showed a normal circular rugal pattern. No dilatation or reservoir function of the prestomal ileum was evident.

A subsequent report on the observations on ileostomy dysfunction will be presented by the authors. —*D. N. Dysart, M.D.*

Poppel, M. H., Abrams, R. M., Handelsman, J., and Segal, A. Diaphragmatic herniation of the pancreas. *Radiology*, July, 1954, *63*, 91–93.

Diaphragmatic herniation of the pancreas, diagnosed preoperatively on roentgenograms, has not been previously reported. A case history is given which demonstrates the authors' hypothesis that herniation or displacement of the duodenum will be accompanied by similar herniation or displacement of the pancreas. In this instance typical pancreatic calculi could be seen in the right hemithorax, probably secondary to a relapsing chronic pancreatitis. The herniation occurred through what was probably a congenitally weak area in the diaphragm, secondary to a large ovarian cyst. In addition to duodenum and pancreas, herniation of the stomach, small intestine, transverse colon, and omentum also occurred.

The authors point out that diaphragmatic herniation of the pancreas can be diagnosed prior to surgery or autopsy, and that the pancreas is not a relatively fixed retroperitoneal viscus.—*C. L. Stevenson, M.D.*

McDonald, Raymond G., and Evans, William A., Jr. Hirschsprung's disease; roentgen diagnosis in infants. *A.M.A. Am. J. Dis. Child.*, May, 1954, *87*, 575–585.

Hirschsprung's disease is defined by the authors as a congenital obstructive disorder of the bowel resulting from an absence or deficiency of the myenteric nerve plexus. They feel that there is very little reason to question the validity of this etiology of Hirschsprung's disease at the present time. The purpose of their paper is to discuss the diagnosis particularly as it pertains to the roentgen examination.

The study is based on 16 patients and is, in a sense, a continuation of the study of previous authors made on 11 patients in 1946. A striking feature of the first group was the predominant occurrence of the disease in boys. A history of severe constipation dating from the neonatal period is characteristic of the disease. Abdominal distention and vomiting are additional frequent manifestations of bowel obstruction. There may be periods of exacerbation and remission. Paradoxically, there may be episodes of diarrhea which is often a grave manifestation and sometimes a terminal event. There may be also retardation of growth and development, according to the severity and duration of the disease.

Surgical procedures were performed in 11 of the patients. Seven deaths occurred in the series of 16 patients. Evidently the disease manifests a high mortality in early life and relatively few mild cases will survive infancy without some surgical relief of the bowel obstruction. In the microscopic study of the resected bowel a correspondence was found between the level of the obstruction and the site of transition from ganglionic to aganglionic bowel. In some instances the transition was rather sharply demarcated and in others it took place more gradually. In all cases the aganglionic segment terminated distally at the anus.

A barium enema examination is required for a diagnosis. The hydrostatic pressure commonly employed in the barium enema examination will often distend the colon in a normal infant to a very marked degree. Thus the degree to which a colon may be distended or elongated during the examination is of no significance in the diagnosis of the disease. The roentgenologic evidence of Hirschsprung's disease in the infant depends upon a study of the

evacuation of the barium enema and the detection of a persistent disparity in caliber of two segments of the colon.

In the study of the cases, four groups representing four stages of the severity of the manifestations on the basis of the first examination by barium enema were distinguished. In the first group the initial barium enema study showed no appreciable deviation from the normal in the evacuation of the barium mixture or in the caliber of the colon. Two possibilities to account for this negative examination are suggested. The patients may have been in a remission such as is known to occur in the course of the disease, or the manifestations of bowel obstruction may have been such as to be evident when the contents of the colon were solid or semisolid but not when they were liquid as in the administration of a barium enema.

In the second group were 3 cases in which the initial barium enema examination demonstrated an abnormal stasis of barium in the colon with no appreciable disparity in the caliber of the segments. The authors regard any significant degree of stasis of barium as an important early sign in the roentgen diagnosis of Hirschsprung's disease in infancy, and they recommend examinations at twenty-four and forty-eight hours or longer following the enema to determine the degree of stasis.

In group three, the initial barium enema study in infants from two days to seven months of age revealed a slight disparity in caliber of two segments of the colon, indicative of the disease. This was best demonstrated by a combined examination in the sagittal, oblique, and lateral projections made at intervals during the evacuation of the barium enema. If doubt then exists as to the presence of a disparity in caliber or as to the location of the zone of transition, the examination is repeated after a lapse of weeks or months, for it is characteristic of the disease that the disparity in caliber of the segments becomes more marked with the passage of time. Progressive dilatation of the proximal segment was demonstrated particularly in some of the patients. However, many cases may be expected to die before any pronounced degree of dilatation and hypertrophy of the proximal segment has occurred. Thus, there may arise the paradoxical situation that the largest colons will be observed in the mildest forms of the disease.

In the fourth group of cases, a typical Hirschsprung's disease of the classic type with a marked disparity in the caliber of the segments was observed at the first examination. This observation was made in an older age group (1 year, 15 months, and 6 years). Where a marked dilatation of the colon already exists, the suggestion of Neuhauser should be followed and only a small amount of barium should be injected to visualize the lowermost portion of the dilated segment. In this manner the length of the aganglionic segment will be demonstrated to better advantage, and there will be less danger of impaction of barium.

In their conclusions the authors emphasize that the roentgen examination by barium enema may be negative in early mild cases of Hirschsprung's disease. The earliest roentgen sign appears to be an abnormal stasis of barium in the colon. A disparity in caliber between the ganglionic and aganglionic segments of the colon may be expected to appear later and to progress, depending on the duration and severity of the obstruction. This is best demonstrated by studies in various projections at intervals during evacuation of the barium.—*Ralph S. Bromer, M.D.*

Theander, Georg. Cholegraphy in children. *Acta radiol.*, July, 1954, *42*, 11–16.

Visualization of the gallbladder and bile ducts, even with priodax, has been unsuccessful in infants younger than six months and unreliable in children under four years of age. The author, however, has had considerable success with biligrafin.

In 11 children, twelve days to two years old, the contrast medium was administered intravenously in a single dose varying from 0.1 to 0.3 gm. per kilogram body weight. One of the children had retrolental fibroplasia, 7 were Mongolian idiots, 1 had atresia of the biliary ducts, and 2 were normal. There was no visualization in the child with atresia of the biliary ducts and in 1 of the Mongolian idiots. In the others, the gallbladder was visualized in from one to seventeen hours after the injection, and in one of these, the common bile duct and hepatic radicles were also opacified. There were no toxic reactions.—*George Cooper, Jr., M.D.*

Orloff, T. L., Sklaroff, D. M., Cohn, E. M., and Gershon-Cohen, J. Intravenous choledochography with a new contrast medium, "Cholografin." *Radiology*, June, 1954, *62*, 868–870.

"Cholografin" is the disodium salt of N:N^1 adipic-di (3-amino-2:4:6-triiodophenylcarboxylic acid).

About twenty minutes after intravenous injection of 40 cc. of 20 per cent solution, the common duct fills and can be demonstrated roentgenographically. Multiple film studies with different degrees of rotation in both the erect and recumbent positions and in lateral decubitus are helpful in separating ribs and gas shadows from the main hepatic and common ducts. Reactions of slight nausea, dizziness, sneezing and restlessness may occur.

The use of cholografin with hyperbilirubinemia and/or lowered hepatic function, especially if associated with jaundice, is not recommended. Common duct calculi were visualized in 3 of the 30 postcholecystectomy patients. In cases of sphincteric relaxation, the concentration of cholografin in the common

duct can be improved with intramuscular injection of ¼ gr. of morphine sulfate.

Figures demonstrating the visualized common duct are included.

The original papers on this new medium are abstracted rather fully in this issue of *Radiology* (pp. 903–905).—*E. E. Seedorf, M.D.*

Steinbach, Howard L., Crane, Jackson T., and Bruyn, Henry B. The roentgen demonstration of cirrhosis of the liver with fatty metamorphosis; report of a case due to congenital fibrocystic disease. *Radiology*, June, 1954, *62*, 858–861.

The authors present a case of congenital fibrocystic disease with associated cirrhosis of the liver in which the diagnosis of cirrhosis was established entirely on the basis of the plain roentgenogram of the abdomen.

The roentgenograms showed multiple poorly defined areas of decreased density superimposed upon an enlarged liver shadow. These were felt to represent large, irregular areas of fat replacement within the cirrhotic liver. The difference in density between the relatively radiolucent fat deposits and the dense fibrosis in the liver suggested the diagnosis.—*Michael J. Healy, M.D.*

Scott, M. Gilbert, Pygott, F., and Murphy, L. The significance of gas or barium in the biliary tract. *Brit. J. Radiol.*, May 1954, *27*, 253–265.

The significance of gas or barium in the biliary tract, other than that due to infection, with gas forming organisms is discussed. A collection of 10 cases seen in a period of three years is reviewed and analyzed. The following causes were reported:

1. Six were due to regurgitation to the sphincter of Oddi. Persistent incontinence of the sphincter of Oddi is thought to be most often due to damage following the passage of gallstones through it, though other causes may be responsible. In one case the presence of gas in the biliary tract was associated with small bowel obstruction and when the patient was explored a fairly large gallstone impacted in the jejunum was found.

2. Two were due to a biliary fistula which may be either cholecystoduodenal or gastric.

3. Two were associated with operative anastomosis. The authors conclude that when gas is present in the biliary tract following cholecystoduodenal or gastric anastomosis there is good evidence that the stoma has remained patent.

Patency of the sphincter of Oddi may be either temporary or persistent. In one case it was present for four and a half years; in another it was only shown during the time the patient was obstructed due to an impacted gallstone in the jejunum.

Previous literature on the subject is also briefly reviewed and adhesions following traction on the sphincter of Oddi, tumors producing induration of the sphincter and keeping it patent, marked antiperistalsis of the duodenum, disturbance of the innervation of the spincter with consequent dilatation were mentioned as other causes of gas or barium in the biliary tract.

A classified list of recorded cases is included.—*P. B. Parsons, M.D.*

Gynecology and Obstetrics

Vogt, Clifford J. Hysterosalpingography—a safe diagnostic and therapeutic gynecological procedure. *Am. J. Obst. & Gynec.*, June, 1954, *67*, 1298–1306.

A general discussion of hysterosalpingography is presented, emphasizing that it is a safe procedure providing a method for positive and definite diagnosis, and shows a high degree of therapeutic effectiveness.

The examination is performed following menses but before ovulation, and is contraindicated in the presence of purulent cervicitis or vaginitis, uterine bleeding, pregnancy, and in acute or subacute pelvic inflammatory disease.

The results of 260 examinations of 213 patients are reviewed. A therapeutic response is assumed because of 166 pairs, showing no absolute factors precluding pregnancy, 109 conceived within six cycles following hysterosalpingography.—*John F. Weigen, M.D.*

Fochem, D., and Ulm, R. Untersuchungen über die Gewebsreaktion bei Hysterosalpingographien mit wasserlöslichen Kontrastmitteln. (Investigation of tissue reaction in hysterosalpingography with water soluble contrast media.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, May, 1954, *80*, 635–638.

The recent world literature contains reports on the favorable use of water soluble contrast material in hysterosalpingography. The objections to the oil contrast substance in this examination have been slow absorption with the danger of renewed closure of the tubes, and the danger of fat emboli.

Three cases are reported in which a water soluble contrast material was used in hysterosalpingography to show that, even with the entrance of the substance into the genital blood vessels and lymphatics of the uterus, there was no complication. This material is absorbed rapidly and the examination may be completed after thirty minutes, in contrast to the twenty-four hour study when the oil substance is used. All of the 3 patients were followed for fourteen days and were asymptomatic at that time.

Experiments were conducted by injecting the water soluble contrast medium into the abdomen

and into the abdominal wall of rats. Upon opening the abdomen, a certain amount of clear fluid was found in the peritoneal cavity up to eight hours after the injection. Roentgen examination of the fluid at various time intervals demonstrated that as early as thirty minutes after the injection, no contrast material could be detected in the peritoneal fluid.

Histological study showed no appreciable pathological changes in the abdominal wall or peritoneum. No inflammatory process could be made out.

The danger of complications from an acute infectious process of the genital system when the hysterosalpingography is done is still to be borne in mind.—*Samuel Richman, M.D.*

Hártley, J. Blair. Incidence and significance of placental calcification. *Brit. J. Radiol.*, July, 1954, *27*, 365–380.

Accurate study of placental site location, antenatally, has been woefully delayed. This seems to have been due to persistent belief in the value of relatively high kilovoltages, without selective filters, and to failure to realize the necessity for really adequate compression of the mother; to faith in professorial demonstration of the fallacies of the methods of other nations; and to the use of relatively long exposures. The author generally reviews and evaluates placentography. The value of roentgenographic demonstration of placental calcification is stressed.

Technical details for roentgenographing the placenta both before and after birth are given and the incidence of placental calcification antenatally after the thirty-second week is shown. These figures are compared with the incidence in placentas roentgenographed.

The relative value of more elaborate methods of assessing placental site (such as aortography, retrograde catheterization of the femoral artery, or use of radioactive isotopes) is stated. It is claimed that they pale into insignificance compared with first-class soft tissue roentgenography, using low kilovoltage technique.

It is claimed that if placental calcification of gross and of medium degrees only can be identified routinely this can enable the roentgen "diagnosis" of the placental site and extent to be correct in 98 per cent of those cases (after 32 weeks) in which this is asked for or required.—*Eugene J. McDonald, M.D.*

Genitourinary System

Wickbom, Igmar. Pyelography after direct puncture of the renal pelvis. *Acta radiol.*, June, 1954, *6*, 505–512.

A method for examination of the renal pelvis is presented by which the contrast medium is injected directly into the renal pelvis by percutaneous puncture. The method is used mainly in those cases where no excretion of medium is seen from one kidney during urography and in which the appearances on aortography are compatible with hydronephrosis or an avascular tumor. Especially in males is retrograde pyelography a complicated procedure and it cannot be employed in those instances where there is complete obstruction of the ureter. In addition, the author believes that the risk of spreading urogenital tuberculosis where urography gives poor results due to impaired function could be diminished by this method.

A long, thin needle is inserted in the best site for puncture, as determined by posteroanterior and lateral roentgenograms using two metal rods placed at right angles to each other on the skin of the back. Five illustrative cases are presented, all having a moderate degree of hydronephrosis with no visible excretion on urography and in which aortography failed to give a definite diagnosis. At operation, no adverse effects of the puncture were noted except for small hemorrhages in the adipose tissue around the kidney in one case. From the results in these cases, the method seems harmless.—*Thomas F. Meaney, M.D.*

Burns, Edgar, and Hendon, Robert G. Aortography as an aid in the management of renal lesions. *Ann. Surg.*, May, 1954, *139*, 617–623.

The authors have performed more than 300 aortographic studies for renal diagnosis without serious complications, employing diodrast and neoiopax (12 cc.) or urokon (25–30 cc.). They stress the importance of this procedure in determining the state of kidney circulation before operating for various benign renal lesions such as hydronephrosis, obstructing renal calculi, renal tuberculosis, and fused kidney. In such cases, aortography helps to establish whether the kidney is worth saving at all, and how much parenchyma might need to be resected. They also state that many small tumors, producing only suggestive calyceal displacements on conventional urograms, can be conclusively identified by renal arteriography.

A retrograde femoral aortogram in a nine month old child demonstrated congenital aneurysms of the right renal artery as the cause of a Goldblatt type of hypertension. In a thirteen year old boy, a right adrenal pheochromocytoma was clearly identified by translumbar aortography.—*Stanley M. Rogoff, M.D.*

Wall, Bithel. Pyelographic changes in necrotizing renal papillitis. *J. Urol.*, July, 1954, *72*, 1–5.

Necrotizing renal papillitis is a well known clinical entity. It has been recognized only recently that there are demonstrable pyelographic changes associated with this condition.

The clinical features of necrotizing renal papillitis are marked upper urinary tract infection, tenderness

in the costovertebral angle, oliguria, and azotemia. The urine shows tissue fragments, in addition to evidences of infection and microscopic hematuria. Most commonly, the condition occurs in female individuals and predominantly in diabetic females. On pyelography the renal parenchymas are symmetrically enlarged. The calyces are irregular in outline and there is evidence of parenchymal destruction with irregularity of the outline of the calyces and in some cases cavitation or abcess formation can be identified.

In one case reported in this article, there was pyelographic evidence of improvement along with clinical improvement following therapy. In another case the roentgen and clinical findings indicated necrotizing papillitis, but a follow-up examination was not obtained. In the third case the surgical specimen of the contralateral kidney showed evidence of necrotizing papillitis, while the pyelographic changes in the remaining kidney showed destructive lesions involving the calyces.

The role of peri-arteritis nodosa associated with sulfonamide reaction is briefly discussed.

The differential diagnosis is chiefly between tuberculosis and necrotizing papillitis. The distinction can usually be made on the cystoscopic and clinical evidence and the lack of any tubercle bacilli in the urine in patients with necrotizing papillitis.—*George W. Chamberlin, M.D.*

Berger, I. R., and Cowart, G. T. Renal echinococcus disease. *Radiology*, June, 1954, *62*, 852–857.

The authors present a case of renal hydatid disease. Findings in this case included a large right upper quadrant mass apparently involving the kidney. Intravenous urograms and retrograde pyelograms confirmed the presence of a mass in the upper pole of the right kidney which distorted the upper and middle calyces. A presacral perirenal pneumography showed the tumor to be intrarenal and suggested adhesions between the renal capsule and the retroperitoneal tissues.

The diagnosis was primarily suspected preoperatively on the basis of previous history of pulmonary lobectomy for echinococcus cyst. The etiology, pathology, symptomatology and methods of diagnosis of this disease are discussed.

Because of its infrequency in the United States, a correct preoperative diagnosis is rarely made. In the cases correctly diagnosed preoperatively, daughter cysts in the urine usually led to the correct diagnosis. In the case presented, the urine was consistently negative for daughter cysts, however. Eosinophilia is almost always present along with a mass, usually nontender, in the renal region. The disease may have a fatal outcome if untreated, nephrectomy usually being essential. Approximately 60 per cent of the cases show cysts elsewhere in the body.

The authors' case terminated fatally postoperatively due to massive pulmonary embolism. Three more cysts were found at autopsy, one retrovesical and two omental.—*Micheal J. Healy, M.D.*

Smothers, W. J., and Siegel, L. H. Rapid identification of urinary calculi through use of x-ray analysis. *J. Urol.*, May, 1954, *71*, 647–649.

This is a brief article pointing out the importance of a rapid method of analysis of urinary calculi, in which a Geiger tube is used to study the diffraction arc. The old method of utilizing the roentgenographic film requires approximately two to three hours for this procedure; but with the use of the Geiger tube the information can be obtained in from fifteen to forty-five minutes.

The article does not explain the technical procedures used, but it does show the roentgen patterns of urinary calculi. One would assume that the procedure employed consists of roentgen-ray diffraction studies of crystallin substances.—*George W. Chamberlin, M.D.*

Elliot, James S., and Rosenberg, Milton L. Ureteral occlusion by barium granuloma. *J. Urol.*, June, 1954, *71*, 692–694.

This is a brief article reporting the single instance of accidental perforation of the lower colon, at the time of a barium enema study. Twenty-four hours following the perforation, a sigmoid colostomy and drainage of the prerectal space was done. The patient was treated with antibiotics and ran a mild febrile course for the next three weeks. Six weeks after the rectal perforation the patient developed oliguria and anuria. The B. U. N. became elevated to 131 mg. per cent. Catheters were passed up each ureter, meeting resistance of 2 and 5 cm. A 6 F catheter was left indwelling in each renal pelvis. Following this, the patient had diffuse diuresis and excreted 4,500 cc. of urine through the catheters within forty-eight hours. At the end of this time her blood chemistry had returned to normal.

Exploration of the retroperitoneal and retrovesical area was performed one week later. In this region there was a fibrotic mass of inflammatory tissue containing tiny streaks of barium observed in the lymphatics. The material appeared to be spread diffusely through the pelvis, and the ureters were incorporated in a dense, inelastic mass. No definitive surgical treatment was possible and the patient had an uneventful convalescence. The ureteral obstruction was then treated by continuous indwelling catheters and ureteral dilatations, following the next six months. There has been no recurrence of the ureteral stenosis and excretory urograms six months and ten months after the initial accident showed normal findings.—*George W. Chamberlin, M.D.*

Bell, Joseph C. Intravenous urography. *South. M. J.*, July, 1954, *47*, 654–659.

The article is a discussion of reactions to contrast media used in excretory urography and a report of 3 cases of tetany and apparent shock, relieved by the use of intravenous calcium gluconate. The results of the report of Dr. Pendergrass to be published in the American Journal of Roentgenology, Radium Therapy and Nuclear Medicine are also presented.—*John F. Weigen, M.D.*

Edsman, Gunnar. Accessory vessels of the kidney and their diagnosis in hydronephrosis. *Acta radiol.*, July, 1954, *42*, 26–32.

The technique used by the author in studying this problem consists of filling the upper collecting systems of excretory urography and turning the patient to the prone position, doing renal arteriography by needle puncture of the aorta. Out of a total number of 388 kidneys he found a normal supply of vessels in 325 kidneys with accessory vessels from the renal artery in 4 kidneys and accessory vessels from the aorta in 59 kidneys, giving a total of 16.2 per cent accessory vessels. Of the patients who had a normal supply of vessels, 23, or 7.1 per cent, had hydronephrosis. Of the 63 patients with accessory vessels 20, or 31.7 per cent, had hydronephrosis. Thus 43 of the kidneys with accessory vessels, or 68.3 per cent, showed no signs of hydronephrosis.

The author concludes that in the group of hydronephrosis with accessory vessels there are probably kidneys present with hydronephrosis which has no connection with the presence of accessory vessels.—*Neal F. Yeomans, M.D.*

Ydén, Sven. Cyst rupture in 6 cases of polycystic renal disease. *Acta radiol.*, July, 1954, *42*, 17–25.

Hematuria frequently causes the adult patient with polycystic renal disease to seek medical advice. Although rupture of the wall of a cyst into a calyx or the pelvis has been reported by several authors, this view is not generally accepted.

The author presents 6 cases of gross hematuria resulting from ruptured cysts. Two of these cases had painless hematuria and the other 4 had rather severe pain associated with the rupture. Five of these cases had direct evidence of a ruptured cyst and 1 had indirect evidence of a ruptured cyst. The typical case had an attack of rather severe pain, followed by hematuria of varying severity. In 5 of the cases the cyst was actually filled with contrast medium. In the other case a defect in the pyelogram caused by a large cyst was seen on original examination which 2½ years later had completely disappeared.

The author found these 6 cases in a series of 26 cases which he reviewed. He concludes that cyst rupture associated with severe pain and followed by hematuria is a fairly frequent event in polycystic renal disease in the adult.—*Neal F. Yeomans, M.D.*

Inman, G. K. E., and Mitchell, J. P. The radiological appearances of a bilateral ureterocele. *Brit. J. Radiol.*, June, 1954, *27*, 350–352.

The authors have reviewed the literature on the demonstration of ureterocele by cystoscopy using various contrast media and techniques. They present one case of bilateral ureterocele that was diagnosed on excretory urography and have come to some very definite conclusions regarding the etiology, appearance on roentgenological investigation, and establishing the diagnosis.

They summarize their findings by stating that ureterocele is an intravesical ballooning of the lower end of the ureter secondary to a congenital stenosis of the ureteral orifice; that the significant feature on a secretory urogram is the ballooning of the distal ends of the ureters which will appear as filling defects in the bladder if the kidney above the ureterocele is concentrating the opaque medium poorly; that the postmicturition film will show the ureterocele unchanged in size contrasted with the reduced bladder shadow; and that cystoscopy will establish the diagnosis in all cases.—*Thomas E. Padgett, M.D.*

Skeletal System

Fullenlove, Tom M. Congenital absence of the odontoid process; report of a case. *Radiology*, July, 1954, *63*, 72–73.

The author presents the ninth case of congenital absence of the odontoid process to appear in the literature since 1933. The patient had a history of trauma to the head six weeks before admission for pain in the left trapezius muscle. Roentgenograms of the cervical spine showed absence of the odontoid process with characteristic flattening of the upper margin of C-2.

The odontoid process is ossified from three centers: two lateral centers, which soon merge, appearing in the fifth month, and one apical center, appearing from the second to the fifth year. Failure of development of the three centers is undoubtedly what appears to produce congenital absence of the odontoid process.—*Michael J. Healy, M.D.*

Gershon-Cohen, J., Budin, Earl, and Glauser, Frank. Whiplash fractures of cervicodorsal spinous processes; resemblance to shoveler's fracture. *J.A.M.A.*, June 5, 1954, *155*, 560–561.

Fractures of the spinous processes in the cervicodorsal area have been termed "clay shoveler's fracture." These occurred in forced laborers working in highway construction in Germany where the

worker was not prepared for the strenuous work he was required to perform. The fracture resulted from a sudden pull from the shoulder via the trapezius, rhomboid, and other thoracoscapular muscles attached to the spinous processes.

A similar fracture was observed in 38 spinal injuries of a total of 480 examinations. Fourteen of these gave a history of riding in a car that came to a sudden stop with a whiplash jerk of the neck. The fractures were due to traction on the interspinous, supraspinous and nuchal ligaments.

Similar fractures were produced experimentally on cadavers.

The fractures tend not to heal and there is often calcification in the soft tissue in this area resulting from a hematoma.—*V. L. Peterson, M.D.*

Plenk, Henry P., and Gardner, Eldon J. Osteomatosis (leontiasis ossea); hereditary disease of membranous bone formation associated in one family with polyposis of the colon. *Radiology*, June, 1954, *62*, 830–840.

Leontiasis ossea is characterized by massive thickening of single or numerous facial or cranial bones. The maxillae, mandible and the frontal and temporal bones are most frequently affected, although the proliferation may involve most of the bones of the skull. Because the etiology is unknown there has been much speculation regarding the origin of this disease. Theories to explain the development of the bony lesions include the following: infectious, traumatic, metabolic, neoplastic, familial and hereditary.

Other investigations have reported the presence of these bony tumors in several members of one family. The authors found 12 cases of multiple osteomas among 64 members of the family with which their article is concerned. Of 14 deceased members, 6 were known to have had bony tumors. Two additional members in generation I and II probably also had tumors. Three members died at eleven, twenty and twenty-nine years of age from accidents. All other deceased members died from carcinoma of the large intestine, proved or suggested, mostly prior to the fifth decade.

A striking coincidence of polyposis of the colon and multiple osteomas was found in living members of this family group of 64. Six deceased members displayed a similar association of the two diseases.

The hereditary pattern of the two conditions, polyposis and osteomas, is suggestive of a single dominant gene responsible for both disturbances.

The term "osteomatosis" is suggested as preferable to leontiasis ossea, since it describes the condition more accurately.—*Arno W. Sommer, M.D.*

Giaccai, L., Salaam, Maria, and Zellweger, H. Cleidocranial dysostosis with osteopetrosis. *Acta radiol.*, May, 1954, *41*, 417–424.

The case history of a twenty-eight year old Arab, who presented signs of cleidocranial dysostosis, osteoporosis and mental deficiency is presented. Defective ossification of the cranial plates with persistence of wide membranous gaps at the sites of the sutures, numerous wormian bones, dental abnormalities with persistence of the deciduous dentition, developmental defects of the clavicles, dysplasia of the phalangeal bones, and hypoplasia of the maxilla and mandible were demonstrated as typical of cleidocranial dysostosis.

Systemic bone sclerosis, brittle bones with multiple transverse fractures, spool-shaped vertebral bodies with condensed epiphyseal plates and persistence of wide vascular channels, and aplasia of the paranasal sinuses were consistent with osteopetrosis.

In addition there was severe mental deficiency. Several other members of the family showed varying degrees of mental deficiency and one brother showed signs of osteopetrosis. No others in the family had cleidocranial dysostosis.

Several instances of co-existing cleiodcranial dysostosis and osteopetrosis were found in the literature. —*Lois Cowan Collins, M.D.*

Meadors, Jason L., and Weens, H. Stephen. Infantile cortical hyperostosis. *Acta radiol.*, July, 1954, *42*, 43–55.

The authors report 8 cases of this condition in Negro infants occurring between the ages of $3\frac{1}{2}$ months and 7 months. In one case there was phalangeal involvement, which has not previously been described to their knowledge, but in the remainder the distribution followed the usual pattern of the disease. The mandible, clavicle and ribs were most often affected.

Laboratory findings proved to be of little value. There may be a delay between the occurrence of soft tissue swelling and the roentgenographic demonstration of bone changes, and conversely there may be roentgenographically visible cortical changes without overlying soft tissue swelling. The etiology remains obscure.

The differentiation of this condition from hypervitaminosis A is important but usually not difficult. In the latter there are lack of mandibular involvement, a history of chronic excessive vitamin A intake and elevated vitamin A blood levels. Metatarsal involvement is common, and characteristically this condition occurs after one year of age in contrast to infantile cortical hyperostosis which is usually encountered during the first half year of life or even in utero.—*Arthur E. Childe, M.D.*

Johnson, John B., Davis, T. Wilkins, and Bullock, William H. Bone and joint changes in hemophilia; a long-term study in twelve Negro subjects. *Radiology*, July, 1954, *63*, 64–71.

Bone and joint changes are the most common manifestations of hemophilia.

Twelve patients with hemophilia were followed. In all, the following laboratory criteria were met: prolonged coagulation time of blood; positive Quick test; normal prothrombin, bleeding and clot retraction times. Several families of patients are included as well as two cousins.

Numerous reproduced roentgenograms of knees and elbows demonstrate the characteristic bone changes. The bone and joint changes in general are the result of decalcification, compression atrophy from hemorrhage, calcium and iron deposition, and fibrous tissue formation with ankylosis.

The earliest joint changes are incident to acute hemarthrosis resulting in a swollen tender joint. Roentgenographic findings are slight or nonspecific.

The moderately advanced stage is the result of chronic irritation from repeated hemorrhages into the joint and is characterized by thickening of the periarticular tissues; hypertrophy of the synovial membrane; erosion of the articular surface of the bone and cartilage; irregularity of the joint space, which may show slight narrowing; widening and deepening of the intercondylar fossa, and early subchondral and intraosseous cystic formation.

The advanced stage exhibits marked diminution or absence of the joint space, pronounced cystic formation, subluxation and sclerosis of the juxtaarticular margins.

The diagnosis of hemophilic arthritis in the acute or early stage is almost impossible by roentgenographic examination alone, while in the advanced stages differential diagnosis may frequently be made. The characteristics of this disease are described, differentiating it from hypertrophic, rheumatoid, gouty and tuberculous arthritis.—*E. E. Seedorf, M.D.*

Harms, I. Über die familiäre Akroosteolyse. (Concerning familial acro-osteolysis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, June, 1954, *80*, 727–732.

Because of the relatively rare occurrence of familial acro-osteolysis (only 72 cases have been recorded) such a case report is added to the literature.

In an eleven year old girl, painless ulcers of the great toes were followed by bone destruction and sequestra. Very few, if any, general symptoms were evident and other diseases having a similar roentgen appearance were ruled out. During the course of five years, extensive destruction of the phalanges and metatarsals of both feet took place, resulting in gross deformity of the feet. A sister of the patient had suffered from the same disease, as well as a brother of the father.

The disease is hereditary and begins in childhood or early adolescence. The bone destruction and absorption progresses in proximal direction, first attacking the distal phalanges of the toes. There are always disturbances in sensory innervation of feet and legs. The roentgen findings, when not complicated by a secondary osteomyelitis, are purely osteolytic with primary concentric bone atrophy of the shafts of the phalanges and metatarsals. The prognosis is favorable as to life, but not as to function of the feet.—*Hans W. Hefke, M.D.*

Turano, Andrew F., Fagan, Katharine Antoinette, and Corbo, Paschal A. Variations in clinical manifestations of osteopetrosis; report of two cases. *J. Pediat.*, June, 1954, *44*, 688–694.

Two cases of osteopetrosis are reported and the wide range of the clinical manifestations is stressed.

One case suggested a malignant lesion and because of roentgenographic evidence of periosteal bone formation first a diagnosis of acute leukemia was made. After a period of four months, during which repeated transfusions were given, roentgenograms showed generalized increased bone density especially in the basilar portions of the skull and in and around the orbits. Roentgenographic survey of the mother and a maternal uncle showed increased bone density in the base of the skull in these two relatives, but other relatives had normal bones. This case terminated fatally after a temporary clinical remission following ACTH therapy.

The second case of a benign type was characterized by malnutrition and growth retardation. Roentgenograms of the parents were negative for bone abnormality. Bone density in this patient was most prominent in the base of the skull, especially the clinoid processes. "Clubbing" of the proximal portion of the humerus and distal portion of the radius and ulna, bilaterally was also noted.

In the first case, the serum acid phosphatase was persistently elevated. This relationship has been reported previously, the significance or correlation with osteopetrosis being unknown. Consanguinity was not present in either case.—*Chauncey N. Borman, M.D.*

Keats, Theodore E., and Bagnall, William S. Chronic idiopathic osteoarthropathy. *Radiology*, June, 1954, *62*, 841–844.

The authors report a case of idiopathic hypertrophic osteoarthropathy. This patient, a 29-year-old Negro soldier, has been followed for a period of six years, without evidence of significant progression of disability or the appearance of underlying disease. Clubbing of the fingers and toes had been present as long as the patient could remember. Pain in the knees and lower legs had been present since the age of sixteen years. Roentgenograms demonstrated diffuse thickening at the cortex of both tibiae. Irregular periosteal proliferation was seen about the malleoli. Similar changes were present in the distal radii.

Chronic idiopathic hypertrophic osteoarthropathy

is a self-limited disease, occurring predominantly in males. Signs and symptoms become manifest in adolescence. Clubbing of the fingers is present in every case. The joints of the extremities are stiff, swollen, painful and enlarged, with some associated soft tissue edema or thickening of the subcutaneous tissue.

The differential diagnosis consists chiefly in distinguishing this condition from secondary osteoarthropathy. Roentgenologically the findings are identical. The absence of demonstrable underlying disease, the onset in puberty, familial influence, and long course all point to the idiopathic form.—*Arno W. Sommer, M.D.*

King, Richard E., Blalock, J. C., and Lovell, Wood W. An unusual spine lesion, possibly typhoid; report of a case. *J. Bone & Joint Surg.*, July, 1954, *36-A*, 863–866.

Careful perusal of the current orthopedic reference works reveals that most authors refer to the typhoid spine briefly, as though it were a relic of the past. In view of this the authors of this article report a case as a reminder that the disease and its complications are still with us and must still enter into our differential diagnosis. Their patient was a sixty-three year old male. His history and physical signs were those described in case reports in the literature.

Comparatively few clinical signs of diagnostic significance are found in this condition. The pain is excruciating, every movement of the spine causing increased suffering. Associated with the pain is severe spasm of the paravertebral muscle groups which serve to splint the involved vertebral bodies.

The roentgenographic appearance is usually believed, according to the authors, to be diagnostic. In previous case reports the diagnosis was definitely made on the basis of roentgenograms alone. The destructive changes in the bodies are seen early; occasionally, there is thinning of the intervertebral discs between the bodies involved. Later, new bone deposits are seen around the vertebrae which form clasplike projections connecting the bodies. Today, however, one might feel less positive in the diagnosis without further laboratory studies.

The most important aid in establishing the diagnosis is the Gruber-Widal reaction. The treatment advised in previous case reports was bed rest; this resulted in improvement and consequent spontaneous fusion. The natural course of fusion can be hastened by surgical fusion. This was done in the case reported in this article. Chloromycetin was not utilized fully in their case.—*Ralph S. Bromer, M.D.*

Farkas, Aladár. The pathogenesis of idiopathic scoliosis. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 617–654.

In this very complete and interesting study of the pathogenesis of idiopathic scoliosis, the author states that he has kept in mind throughout the study of the condition the distinction between the underlying mechanical factors and the basic pathological process. He has well summarized his findings which are as follows:

1. Scoliosis has four fundamental characteristic features as seen in the roentgenograms: Penetration or a transverse shift of the spine into the space surrounding it; contracture of the spine; rotation of the vertebrae; and compression of the vertebrae on the concave side of the curve.

2. Penetration and compression are the essential scoliotic signs and are not encountered under physiological conditions.

3. The prevention of penetration is physiologically carried out by a passive mechanism.

4. The universal mechanical factor of all forms of acquired scoliosis is human gait, which in the presence of a definite pathological process brings about the deformity.

5. Rotation of the shoulders and of the trunk, or of the pelvis, is accompanied by rotation of the spine in the opposite direction.

6. The compression on the concave side is a primary characteristic of idiopathic scoliosis in the thoracic spine.

7. The vertebra is protected against undue compression by the disk, by the cartilaginous plate, and by the vertebral cortex which is composed of the end plates covering the upper and lower surfaces, of the circular bony hull, and of the epiphyseal ring.

8. The separation of the vertebral cortex from the intravertebral system, notably the separation of the epiphyseal ring and its partial displacement, represents the basic pathological process of idiopathic scoliosis in the thoracic spine. Separation is preceded by the infantile (juvenile) form of osteoporosis of the spine.

9. Posteroanterior roentgenograms reveal the presence of channels crossing the vertebrae in a frontal direction.

10. The compressed vertebrae, as seen in the early stages, consist of two distinct portions: One is an ossified and porotic part, the core; the other, surrounding it or lying beside it, is a poorly or noncalcified, still more or less cartilaginous, portion.

11. In a typical case, idiopathic scoliosis of the thoracic spine starts in the cervicothoracic segment, and several years may pass before the middle and lower thoracic regions become involved. The process in the uppermost region presumably begins in the first four years of life.

12. Penetration and lateral movements, to the extent observed in scoliosis, are caused partly by subluxation in the articulations between the vertebrae.

13. Since idiopathic scoliosis of the lumbar spine is essentially of a rotatory nature without compression, a distinction is made between idiopathic scoliosis of the thoracic and lumbar spine.

14. Idiopathic scoliosis of the lumbar spine is made

possible by congenital anomalies in the articular system of this region. The disappearance or decrease of the lumbar lordosis materially contributes to the development of the deformity.

15. Extrusion of the epiphyseal ring, if it occurs at all, is mostly a late phenomenon in the lumbar region.

16. The lumbar type of idiopathic scoliosis is characterized by rotation in the same direction of all vertebrae involved.

17. The prognostically most serious cases are those in which congenital anomalies in the lumbar segment are combined with the pathological process encountered in the thoracic type of deformity.

The article contains 27 illustrations, many of which are reproductions of roentgenograms.—*Ralph S. Bromer, M.D.*

Silverman, Frederic N. Calcification of the intervertebral disks in childhood. *Radiology*, June, 1954, *62*, 801–816.

Seven new case reports of children with intervertebral disk calcification, and comparison with 8 reports available in the literature are presented. In the author's opinion, there is no constant relationship between clinical complaints and intervertebral disk calcification. Age, duration and location are not particularly valid criteria for evaluating the nature of disk calcification, and factors accounting for the appearance, persistence, or disappearance of the calcification are unknown. The one fact that persistent calcifications have not been recognized in the cervical levels may permit separation of the group with transient cervical calcification and neck pain from the group with persistent or disappearing calcification in other regions.

Intensive treatment in the presence of symptoms referable to the level of calcification is not justified. —*A. Ralph Watson, M.D.*

McFarland, Bryan. My present attitude to osteo-arthritis of the hip. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 476–488.

In his introductory paragraph, Prof. McFarland states he does not know the best treatment for osteo-arthritis of the hip. In fact he does not know that there is a best treatment. His theme is that when an operation becomes necessary, the procedure to be picked must be the one most appropriate to a particular patient. Easy, attractive and immediately satisfying though the new technique of arthroplasty may be, it is neither justifiable nor possible to discard other well tried operative methods. There are patients for whom each of these methods may be the most suitable. Arthroplasty is unlikely to endure unless more is learned about the origin of pain and unless materials are used which are more natural to, and conform more closely with, the tissues of the human body. The elaboration and illustration of this theme follows in his article.

The article is illustrated with numerous roentgeno grams showing results of types of operations performed for osteo-arthritis of the hip, with also clinical photographs.—*Ralph S. Bromer, M.D.*

Nicholson, Jesse T., Kopell, Harvey P., and Mattei, Frank A. Regional stress angiography of the hip; a preliminary report. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 503–510.

This study of regional stress angiography of the hip was undertaken as a means of visualizing a suspected diminution in blood supply which may result from placing the limbs in the "frog-leg position." This position is commonly used to maintain the reduction of a congenital dislocation of the hip. The hips are held in abduction of approximately 90 degrees, flexion of 90 degrees, and external rotation of 90 degrees. The medium injected consisted of a mixture of barium sulphate and lead chromate suspended in a 10 per cent solution of vinylite (copolymer of acetate and chloride) in acetone. In all cases, injections were performed within twenty-four hours after death.

The experiments were divided into two parts. In the first part the injections were made into the abdominal aorta while one leg was held in the frog-leg position and the other in the neutral position. After a sufficient time had elapsed for the injected mass to set, both extremities were placed in the anatomical position for roentgenographic examination. In the second part of the experiment both extremities were held in the frog-leg position, and a subcutaneous adductor tenotomy was performed on one side. The injection into the abdominal aorta followed the adductor tenotomy. The roentgenographic examination was made with the lower limbs in the anatomical position. Subsequently it was found that better visualization of the arteries was obtained when the limbs were internally rotated during the roentgenographic examination.

In their summary, the authors state that there is reason to believe, on the basis of angiography in autopsy material, that the frog-leg position interfered with arterial filling in the hip area. This effect appeared more marked in the presence of adductor resistance. The arteries affected by the position were the medial femoral circumflex, the laterial femoral circumflex, and the profunda femoris. Adductor tenotomy proved to be an aid in abolishing the effect of the frog-leg position upon the arterial circulation to the hip area.—*Ralph S. Bromer, M.D.*

Heyman, Clarence H., and Herndon, Charles H. Epiphyseodesis for early slipping of the upper femoral epiphysis. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 539–555.

The operation employed by the authors for slipping of the upper femoral epiphysis is illustrated by line drawings. A piece of cortical bone is removed from the neck of the femur which is to be replaced later. A hole, 1 cm. in diameter, is drilled across the center of the epiphyseal plate. Small pieces of cancellous bone from the crest of the ilium are impacted into the hole and are driven across the epiphyseal plate, or a solid piece peg of cancellous bone may be driven in. The piece of cortical bone which was removed from the neck of the femur is replaced in its original position and the periosteum is sutured.

The article is illustrated with numerous roentgenographic reproductions showing progress of fusion and end results. Roentgenograms made soon after operation reveal a moderate but temporary demineralization throughout the epiphysis as compared with a relatively increased density before operation. This the authors regard as indicative of a good blood supply. In one case in which a drafting procedure was done at the time of open reduction of an acute slipping, there had been sudden and complete displacement of the epiphysis, which was isolated from any supply other than that provided by the ligamentum teres. Fusion was present at the end of eleven weeks in this case and the roentgenographic appearance and the function of the hip when the patient was last seen were normal.

For those who are not satisfied with metallic fixation or with conservative treatment, the grafting procedure is recommended as it unquestionably, according to the authors, stimulates prompt fusion of the epiphysis. The average time for fusion after operation, in their cases, was 2.3 months, as compared with 19.8 months reported in patients treated by conservative measure and as compared with the doubtful hastening of fusion by metallic fixation.—*Ralph S. Bromer, M.D.*

Lichtblau, Philip O., and Thompson, T. Campbell. A femur with two heads and necks; a case report. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 610–616.

In the introductory paragraph of this article, the authors state that adequate roentgenographic studies prior to reconstructive hip surgery are mandatory. They are required for the selection of the surgical procedure of choice. They may also obviate the necessity for further surgical intervention.

The patient whose case history is reported in this article was a boy of seven years of age who came to the Orthopedic Clinic because of a limp on the left side. The past history revealed that at one and one-half years of age he had fallen and injured his left hip. He was taken to a hospital where an inflammatory process of the hip was treated by incision and drainage. He was hospitalized for nine months.

Roentgen examination on his admission to the Clinic showed a poorly developed acetabulum and femoral head and neck on the left side. The upper femoral shaft was displaced widely outward and upward, the head of the femur apparently resting against the iliac wing. Push-pull roentgenograms revealed vertical instability, but the tip of the femur could not be brought down to the level of the acetabulum. No exposures were made with the hip in internal and external rotation. The presumptive clinical diagnosis was dislocation of the left hip, secondary to an old infectious arthritis.

A Colonna hip reconstruction was performed. The patient was discharged two months after operation when he was walking well with crutches. He was last seen five months after operation; at that time he was walking well without crutches. The postoperative roentgenograms demonstrated the presence of two heads and necks on the femur, the lower head being in good relation to the acetabulum.

In retrospect, had roentgenograms of the hip in internal and external rotation been made before operation, the pathological entity would have been discovered preoperatively. The authors know of no similar case described in the literature. They suggest that the central portion of the upper epiphyseal plate had been destroyed during the active infectious process, assuming that the history was correct. Subsequently, with further growth, two separate heads and necks developed. Dislocation probably occurred at this time or shortly after weight-bearing was resumed. In having placed the lower femoral head in the acetabulum, the more developed and normal looking head was unknowingly inserted in the acetabulum. It was anteverted almost 90 degrees in relation to the upper femoral head. It has been suggested that, if the upper femoral head had been placed into the acetabulum, additional length would have been gained. At present, the authors found the functional and roentgenographic results quite satisfactory.—*Ralph S. Bromer, M.D.*

Clark, John M., and Jacobson, George. Congenital coxa vara; osteochondrodysplasia of the femoral neck. *Radiology*, July, 1954, *63*, 59–63.

Congenital coxa vara is a deformity of the hip caused by osteochondrodysplasia of the femoral neck. The etiology has never been definitely established. The occurrence of the process as a solitary lesion tends to exclude a generalized metabolic disorder, such as rickets, as an etiologic factor. The condition must be differentiated from fracture of the femoral neck, Legg-Perthes' disease, slipped femoral epiphysis and coxa vara following localized infection.

Coxa vara is present in most cases of osteochondrodysplasia of the femoral neck and is the most readily discernible manifestation of the disease. The epiphyseal plate assumes a more vertical position than is normal. The femoral neck adjacent to the epiphyseal plate is frequently fragmented. Char-

acteristically, a triangular fragment of bone is seen just beneath the capital femoral epiphysis. As the deformity progresses, the neck is shortened or may be completely absent. Fusion of the femoral head occurs at the level of the lesser trochanter. In advanced stages a pseudarthrosis may result.

Proper treatment leads to uniformly good results, whereas untreated cases often progress to crippling deformities. Subtrochanteric wedge osteotomy appears to be the preferred method of treatment.—*A. W. Sommer, M.D.*

Milch, Robert Austin. Roentgenographic study of the inclination of the lateral pelvic wall and the interacetabular distance in normal adult pelves. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 533–538.

The human pelvis may be divided into four general types: android (male), gynecoid (female), anthropoid (ape) and platypelloid (flat). Most of the anatomical features which permit differentiation of these four types are those of the interior of the true pelvis, of the anteroposterior and transverse diameters of the pelvic inlet, the mid-pelvis and the pelvic outlet. This classification of the pelvis is virtually of exclusively obstetrical concern. According to the author, the exterior of the pelvis, which is of no obstetrical importance has received only minimal attention. Practically no information is available concerning either the lateral pelvic wall or the interacetabula distancer.

The proper mensuration of these latter anatomical entities, however, is of importance to the orthopedic surgeon. It has been clearly shown that angle of inclination of the lateral pelvic wall directly determines a critical value for the angle of the mechanical neck of the osteotomized femur (the postosteotomy angle) beyond which increasing stability results in concomitantly decreasing mobility at the hip. Milch further states that the apparent lengthening resulting from unilaterally performed osteotomy of the upper femur (when the contralateral hip is freely movable) is directly related to the length of the interacetabular line and to the angle formed between the interacetabular line and a line drawn perpendicular to the mechanical axes of both erect and parallel femora.

This study was undertaken by the author to discover (1) whether or not there is any relationship between these entities of the exterior of the pelvis and those of the interior, in relation to the four fundamental types, and (2) whether or not there is any significant difference between these external measurements for pelves of adult men and women. One hundred anteroposterior roentgenograms of normal female pelves and 100 roentgenograms, anteroposterior projection, of normal male pelves were studied. No significant difference was found among the angles of the pelvic wall in any of the four primary types of pelves. The difference in mean interacetabular distance and the mean angle of inclination of the lateral pelvic wall between male and female subjects was statistically highly significant ($P<0.001$). Milch suggests that there is no correlation between the distinguishing anatomical features of the interior of the true pelvis and those of the exterior of the pelvis. He further suggests that the difference in clinical hip width among male and female subjects, respectively, is not due to the anatomical features of the true pelvis. He presents data for the statistically probable maximum and minimum amounts of apparent change in limb length which can be expected in virtually all patients following upper femoral osteotomy performed for unilateral hip disease.—*Ralph S. Bromer, M.D.*

Selakovich, Walter, and Love, Leon. Stress fractures of the pubic ramus. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 573–576.

Five cases of stress fracture of the pubic ramus are described in this article. The precipitating factor in production of these stress or march fractures is undoubtedly unusual physical activity in a formerly sedentary individual. The condition is probably the result of pull and strain of the adductors and the hamstring muscle groups with an associated adductor pull, more anteriorly, on the inferior pubic ramus. Recruits in the army first noticed pain in the inguinal, perineal, and adductor regions, bilaterally, with tenderness on palpation of the inferior pubic ramus.

Roentgenographic examination reveals a definite break in the continuity of the cortex. It is usually an irregular break in a vertical direction through both cortices, and calcification of a moderate degree surrounds the area. As healing progresses the fracture fissure gradually diminishes and the calcification increases.

The authors suggest that this condition be borne in mind as it may aid in avoiding a mistaken diagnosis of benign or malignant tumor and unnecessary surgical exploration.—*Ralph S. Bromer, M.D.*

Martz, Carl D., and Taylor, Clifford C. The 45-degree angle roentgenographic study of the pelvis in congenital dislocation of the hip. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 528–532.

Routine roentgenographic studies of congenital dislocation of the hip demonstrate clearly the superoinferior and mediolateral displacements of the femoral head, but the vital dimension of depth in which anterior and posterior displacements occur is not readily visualized. Lateral views are found to be frequently unsatisfactory because of the superpositioning of other structures. Furthermore, stereoscopic views are not practical for active infants. For these reasons, the authors use an anteroposterior, 45

degree cephalad view. Clear films are possible no matter what position of the limbs is selected. Standard roentgenographic equipment and techniques are used. The anatomical landmarks are those ordinarily employed and the spine of the femoral neck may be used as a landmark in the early months of life before the ossification center of the head appears. Many of the classically described relationships are visualized in this angled view.

The patient, in their method, is placed flat on his back. The lower extremities should be fairly symmetrically placed but abduction, flexion and rotation of the extremities are at the pleasure of the surgeon. A routine anteroposterior roentgenogram of the pelvis is made and then a 45 degree cephalad exposure is made with the tube still centered on the symphysis pubis. The anteroposterior roentgenogram reveals superior or lateral displacement of the femoral head in relation to the acetabulum. The 45 degree cephalad roentgenogram reveals anterior or posterior displacement. When the head is anterior to the acetabulum, its shadow on the angled view is closer to the top of the roentgenogram then the acetabulum; when the head is posterior to the acetabulum, its shadow on the angled view is closer to the bottom of the roentgenogram. When the head is in the cup of the acetabulum, its shadow is in the cup; when the head is anterior to the acetabulum, its shadow is above the cup; and when the head is posterior to the acetabulum, its shadow is below the cup.

With this method the authors have been able to recognize early those congenital dislocations of the hip which have anterior displacement of the head and they have been able to correct this by proper positioning. Furthermore, by the use of this view they could verify the success of their plan of treatment. They note as interesting that in 50 cases studied over a five year period, when sagittal displacement occurred in the dysplastic hip, it was almost always anterior. One traumatic case proved to be posterior. They state that many of the present surgical techniques are based upon plane diagrams which ignore the third dimension of depth.—*Ralph S. Bromer, M.D.*

KITE, J. H. Torsion of the lower extremities in small children. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 511–520.

Torsion of the lower extremities in small children usually takes one of two patterns. The children may have medial torsion and be bow-legged and pigeon-toed, or they may have lateral torsion and be slightly knock-kneed and flat-footed. The author considers two groups of medial torsion—congenital and acquired—because of difference in etiology and treatment.

In the congenital medial group the children have a marked lateral convexity to the leg, between the knee and the ankle. The deformity is present at birth but may not be recognized then. In roentgenograms of these cases the shadow of the soft part shows a laterial convexity to the lower leg, but the shafts of the tibia and fibula are straight. The metaphyses at the distal ends of the femora and the proximal ends of the tibiae show an expansion of bone on the medial side. Cupping or fraying suggestive of rickets is never seen. There is increased density of the metaphysis adjacent to the epiphyseal line. In some cases this may be slight, while in others it is marked. The angulation which produces the lateral convexity takes place at the epiphyseal line. The change is most marked at the distal epiphysis of the tibia. Instead of the line being perpendicular to the long axis of the bone, it is oblique, facing medially. The tibia is shorter than normal and the fibula is longer.

There may be spontaneous improvement. Conservative treatment is indicated, double braces being applied, should manipulative therapy show no improvement.

In acquired medial torsion, the limbs are straight at birth, but a deformity is produced by the positions of the patient in sleeping and sitting. The roentgenographic findings are similar to those described for congenital medial torsion, but are less pronounced. The deformity is not usually noticed until the child begins to sit and crawl.

Lateral torsion is the reverse of the medial torsion. In addition to the lateral rotation of the lower extremities, there is some knock-knee deformity and usually a servere flat-foot deformity. This group of patients are babies who sleep either on the abdomen or on the back in a "frog-leg" or "spread-eagle" position. A few may sleep in the knee-chest position with the toes turned out in a flat-foot position. Treatment, according to Kite, consists in breaking the faulty sleeping and sitting habits. The parents are also taught proper manipulative procedures. No roentgenographic findings are described in this group.

Unilateral torsion is occasionally found. This is usually an acquired deformity. It is produced by the child sitting and sliding with one foot under him and the other stretched out in front of him. This can be remedied by correcting the sitting habits and by manipulations.

In the paper the physical examination of the groups is described in detail, likewise the treatment. Clinical photographs and roentgenograms are reproduced.—*Ralph S. Bromer, M.D.*

FLEMING, JOSEPH L., and SMITH, HAROLD O. Fracture-dislocation of the ankle with the fibula fixed behind the tibia. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 556–558.

In the case reported in this article, the roentgenograms of the fractured ankle showed in the anteroposterior projection marked posterior displacement of the fibula behind the tibia. To the medial side of

the medial malleolus was a large fragment of bone which, later roentgenograms showed, came from the medial portion of the medial malleolus and was avulsed by the periosteal expansion of the deltoid ligament. Lateral roentgenograms revealed the long spike of the fibula apparently securely lodged behind the posterior flare of the tibia. Marked posterior displacement of the fibula was also noted. After two attempts at reduction excellent position was secured. The reduction was obtained, under anesthesia, by closed manipulation.

For reduction to occur, the proximal fragment of the fibula had to pass from behind, over the posterolateral tibial prominence, to its normal position. In this unusual fracture-dislocation, the authors think it seems necessary to assume either that the main tibiofibular ligaments (the interosseous portion) are somewhat lax or that the posterolateral tibial protuberance is smaller than usual, allowing the proximal fibular fragment to rotate around the tibia. The main tibiofibular ligaments are intact for, if they were ruptured (along with a varying length of the interosseous membrane), there would be nothing to hold the fibular shaft so securely in its posteromedial position.—*Ralph S. Bromer, M.D.*

Dahlin, David C., and Johnson, Einer W., Jr. Giant osteoid osteoma. *J. Bone & Joint Surg.*, June, 1954, *36-A*, 559–572.

Eleven unusual and microscopically characteristic benign tumors have been encountered in a study of pathological specimens in approximately 2,000 cases of primary tumor of bone at the Mayo Clinic. This tumor, which apparently always originates within bone, consists principally of partially calcified osteoid trabeculae in a vascular stroma. The authors have chosen to call this tumor "giant osteoid osteoma" because this name seems most fitting. It is distinctively different from the ordinary osteoma and should not be classed with it.

In the series of 11 tumors, 4 occurred in vertebrae, 5 were found in the long bones, 2 in the femur, 2 in the tibia and 1 in the humerus. Of the 2 remaining tumors, 1 involved the upper fourth of the patella and the other had almost completely destroyed the talus.

Grossly the lesions were homogeneously hemorrhagic, friable, and granular, varying from a reddish color to purple. The specimens were granular and gritty because of the calcifying osteoid which they contained. The tumors were reasonably well demarcated from the surrounding normal or sclerotic bone. On microscopic examination, many sections from all lesions revealed osteoid tissue showing varying usually slight, degrees of calcification, and vascularity was the next most prominent feature. Evidence of malignancy was absent in all cells.

The initial roentgenograms showed definite evidence of lesions of bone in all but one instance, and in this case they subsequently revealed evidence of a lesion. It was impossible to outline a definite set of criteria for diagnosis of this type of benign lesion of bone on the basis of roentgenograms alone. The roentgenograms of 5 patients showed bone destruction only and 3 whose vertebrae were involved were in this group. The roentgenograms of each of the 5 patients having lesions in the long bones showed an area of bony sclerosis and in each a central area of bony rarefaction was seen. In the eleventh case the roentgenogram was interpreted as showing evidence of an osteoma arising from the third lumbar vertebra.

These tumors bear similarities to several other lesions. Osteoid osteoma is the lesion they mimic most closely from the histological standpoint. Several features, however, serve to distinguish them from osteoid osteoma. Among these are the much greater size, more marked vascularity, more orderly pattern of larger osteoid trabeculae, tendency to erode through the cortex, and the inconstancy of the surrounding bony sclerosis. Grossly the tumors were softer and more hemorrhagic than the usual osteoid osteoma.

Aneurysmal bone cysts, as described by Lichtenstein, bear similarity to the authors' type of tumor. In none of their cases, however, were there discrete cavernous vascular channels and blood pools of the type described by him as "showing the essential cavernous character of the lesion."

Osteogenic fibroma of bone seems to contain all the elements found in the tumors reported in this series. If the lesions are identical, the authors are of the opinion that the term "osteogenic fibroma" is an unfortunate one, because the fibromatoid component is the least striking histopathological feature.

Giant-cell tumor is another which might be confused with giant osteoid osteoma. It is probable, Dahlin and Johnson think, that some of the "variants" of giant-cell tumor mentioned in other publications are examples of the tumor they now describe. They regard their cases as distinctly different from giant-cell tumors. The plump, prominent, spindle-cell stroma of giant-cell tumors is lacking. The sites of predilection are different, giant osteoid osteoma occurring in any portion of the bone. Osteoid proliferation in their cases is distinctly unlike the pattern of giant-cell tumor.

The curability of the lesions of the patients of this series, when treated by adequate curettage with or without subsequent radiation therapy, indicates their benign behavior.—*Ralph S. Bromer, M.D.*